AMERICAN JOURNAL
OF
OBSTETRICS AND GYNECOLOGY

ADVISORY EDITORIAL BOARD

FRED L. ADAIR
BROOKE M. ANSPACH
JAMES R. BLOSS
LUCIUS E. BURCH
WALTER W. CHIPMAN
WILLARD R. COOKE
HARRY S. CROSSEN
THOMAS S. CULLEN
ARTHUR H. CURTIS
WILLIAM C. DANFORTH
WALTER T. DANNREUTHER
CARL H. DAVIS
ROBERT L. DICKINSON
PALMER FINDLEY
C. FREDERIC FLUHMANN
ROBERT T. FRANK
WILLIAM P. HEALY
F. C. IRVING
JENNINGS C. LITZENBERG
JAMES C. MASSON
HARVEY B. MATTHEWS
JAMES R. MCCORD
NORMAN F. MILLER
EMIL NOVAK
EVERETT D. PLASS
ISIDOR C. RUBIN
OTTO H. SCHWARZ
PAUL TITUS
HERBERT F. TRAUT
NORRIS W. VAUX
GEORGE GRAY WARD
BENJAMIN P. WATSON
PHILIP F. WILLIAMS
KARL M. WILSON

OFFICIAL ORGAN

THE AMERICAN GYNECOLOGICAL SOCIETY; THE AMERICAN ASSOCIATION OF OBSTETRICIANS, GYNECOLOGISTS, AND ABDOMINAL SURGEONS; NEW YORK OBSTETRICAL SOCIETY; OBSTETRICAL SOCIETY OF PHILADELPHIA; BROOKLYN GYNECOLOGICAL SOCIETY; ST. LOUIS GYNECOLOGICAL SOCIETY; NEW ORLEANS GYNECOLOGICAL AND OBSTETRICAL SOCIETY; BALTIMORE OBSTETRICAL AND GYNECOLOGICAL SOCIETY; CHICAGO GYNECOLOGICAL SOCIETY; CINCINNATI OBSTETRIC SOCIETY; CENTRAL ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS; AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY; WASHINGTON GYNECOLOGICAL SOCIETY; PITTSBURGH OBSTETRICAL AND GYNECOLOGICAL SOCIETY; OBSTETRICAL SOCIETY OF BOSTON; LOUISVILLE OBSTETRICAL AND GYNECOLOGICAL SOCIETY; SOUTH ATLANTIC ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS; SEATTLE GYNECOLOGICAL SOCIETY; SOCIETY OF OBSTETRICIANS AND GYNECOLOGISTS OF CANADA; ALABAMA ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS; AKRON OBSTETRICAL AND GYNECOLOGICAL SOCIETY; KANSAS CITY OBSTETRICAL AND GYNECOLOGICAL SOCIETY; CENTRAL NEW YORK ASSOCIATION OF GYNECOLOGISTS AND OBSTETRICIANS; NEW JERSEY OBSTETRICAL AND GYNECOLOGICAL SOCIETY.

EDITOR

GEORGE W. KOSMAK

ASSOCIATE EDITORS

HOWARD C. TAYLOR, JR. . . . WILLIAM J. DIECKMANN

VOLUME 56

JULY-DECEMBER, 1948

ST. LOUIS

THE C. V. MOSBY COMPANY

1948

COPYRIGHT, 1948, BY THE C. V. MOSBY COMPANY

(All Rights Reserved)

Printed in the
United States of America

Press of
The C. V. Mosby Company
St. Louis

American Journal of Obstetrics and Gynecology

VOL. 56 JULY, 1948 No. 1

Transactions of the Central Association of Obstetricians and Gynecologists. Annual Meeting Held October 23 to 25, 1947, at Louisville, Kentucky

THE EFFECTIVENESS OF VARIOUS DIURETIC AGENTS IN CAUSING SODIUM EXCRETION IN PREGNANT WOMEN*

WILLIS E. BROWN, M.D., AND J. T. BRADBURY, SC.D., IOWA CITY, IOWA

(From the Department of Obstetrics and Gynecology, State University of Iowa)

TOXEMIA of late pregnancy remains the one large cause of maternal morbidity and mortality for which there is no adequate etiologic explanation. Many students doubt that it is a single disease entity and differential classifications have been offered to explain the variety of clinical manifestations. In spite of the extended investigative efforts that have been expended on this syndrome, it still remains a therapeutic enigma, our ministrations being quite empirical.

Edema is one of the most common signs of toxemia, and yet it is not clear whether the accumulation of fluid represents a disorder of water or sodium or protein metabolism. Earlier workers focused attention on water metabolism and treated such patients by manipulations of water intake. Limited investigations in this direction have been complicated by the difficulties in obtaining proper control. During the past two decades the concept that edema may be due to a disorder of sodium metabolism has gained popularity to the extent that the clinical management of toxemias of pregnancy now generally includes a reduction in sodium intake (sodium chloride and sodium bicarbonate).

*Read before Central Association of Obstetricians and Gynecologists on Oct. 23, 1947, at Louisville, Ky.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

Because of the interest in sodium and in the factors involved in augmenting its excretion, a series of studies was undertaken to investigate the effects of so-called diuretic agents on the fluid and sodium excretion in women with normal and toxemic pregnancies.

Water balance studies require a long-time control of intake and output, including the insensible loss of water through respiration and perspiration. Because of these difficulties, several investigators have attempted to study sodium balance. In general, the methods of sodium analysis have been too cumbersome for routine laboratory determinations. Consequently, more work has been done on chloride balance studies on the assumption that there is a definite relation between chloride and sodium. This is obviously incorrect since not all the chloride in the urine and food is sodium chloride. In addition, attempts have been made to investigate the effect of ammonium chloride, where the excess chlorides make chloride estimations entirely unreliable as an index of sodium excretion. A simplified method of sodium estimation developed in this laboratory made it possible to study the effect of various diuretics on sodium output.

Observations were made on pregnant patients given high and low sodium diets. Hourly fractional or total twenty-four-hour urine specimens were obtained and determinations made of the sodium concentration in the urine. From these data, information regarding the mobilization and excretion of sodium have been obtained which may have some direct application in the clinical management of edema of pregnancy.

Methods and Materials

Sodium Method.—There are two basic methods for measuring the sodium content of biologic materials. The physical method makes use of a flame photometer.[1] The substance to be measured is dissolved and burned at a constant volume rate. The intensity of the sodium flame is measured and computed as grams of sodium. While this method has many advantages, the operation of the flame photometer is such a highly technical procedure that its use is not satisfactory for most laboratory technicians.

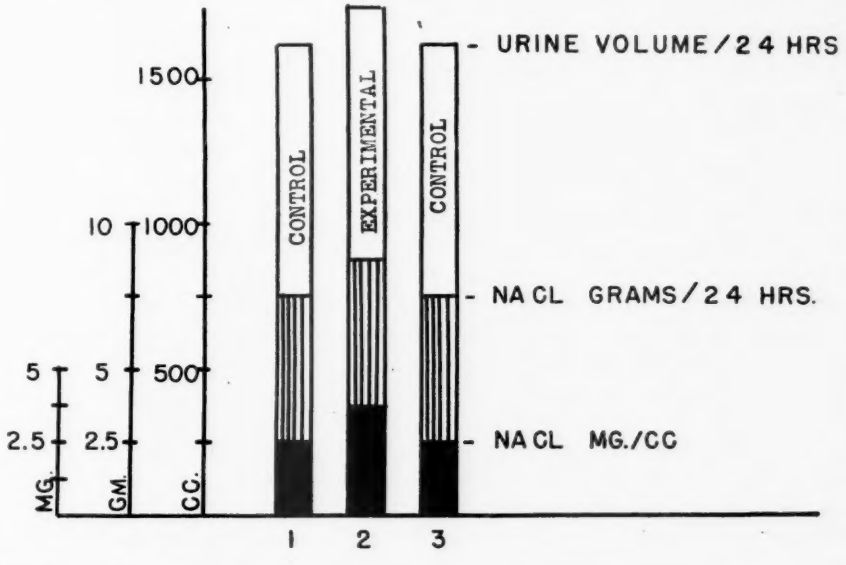
The chemical method involves the precipitation of sodium by uranyl zinc acetate.[2] The quantity of sodium in the precipitate can be determined by gravimetric or colorimetric procedures.

The sodium determinations in this study were made by a colorimetric technique based on the original gravimetric method. When the triple salt, uranyl zinc sodium acetate is precipitated, the reagent solution loses color in proportion to the amount of uranyl ions lost from solution. The loss of color is measured by an electrophotometer and its sodium equivalent is determined from a standard reference curve.[3] In this report all values for sodium are expressed in terms of sodium chloride; the conversion to sodium can be obtained by multiplying all figures by 0.4.

Patient Control.—The patients used in this study were hospitalized in the obstetric wards. Their diets were prepared by the Department of Nutrition and the caloric values and sodium contents calculated from tables. These diets have been varied from low values of 1 to 1.5 Gm. of sodium chloride (0.4 to 0.6 Gm. sodium) per twenty-four hours to normal values of 4 to 6 Gm. per twenty-four hours; higher intakes of 10 to 15 Gm. were achieved by giving the patients additional salt.

The patients were housed in a special ward and their water intake recorded daily. The studies were continued over periods of several weeks. Each patient was given a controlled sodium intake for a minimum of three and usually five days prior to establishment of a treatment schedule. The experimental schedules were generally arranged to correspond to the usual clinical therapeutic plans employed in the hospital. Observations were made on normal and toxemic pregnant patients and on a few nonpregnant women in the childbearing age.

Urine was collected daily as a twenty-four-hour specimen and the sodium content of each was determined. The average values for the specimens three days prior to, and three days following treatment were used as controls and compared with the urine volume and sodium value obtained on the day of the test.



Key to figures:

1. Pretreatment control (1 day or average of 3 days)
2. Day of treatment
3. Post-treatment control (1 day or average of 3 days)

The figures illustrating the text are constructed in the same way as this sample graph.

Materials Studied.—The following substances were selected and studied for their effect on the excretion of water and sodium.

1. Water (by mouth) given in quantities of 2,000 to 6,000 c.c. daily. A few patients received this amount of water in two to four hours.
2. Dextrose (intravenously); given as 5 per cent, 10 per cent, 25 per cent and 50 per cent solutions in amounts varying from 400 to 4,000 c.c. depending upon the concentration.
3. Aminophylline (intramuscularly); given in doses ranging from 120 mg. to 150 mg. daily (1 gr. b.i.d. to 7½ gr. t.i.d.).
4. Mercurial diuretics (Salyrgan (100 mg./c.c.), Salyrgan-theophylline (mercurial 100 mg./c.c. plus theophylline 50 mg./c.c.) and Mercuhydrin (mercurial 88 mg./c.c. plus theophylline 48 mg./c.c.) given intravenously in doses ranging from 2 to 4 c.c.
5. Ammonium chloride (by mouth and intravenously); given in amounts varying from 8 to 16 Gm. per 24 hours.

6. Urea (by mouth); given in amounts of 60 Gm. per 24 hours (20 Gm. in 80 c.c. of water t.i.d.).

All of these substances have some effect on sodium and/or water excretion. The effect varies with the diuretic but each agent follows a fairly consistent pattern.

Data

Effect of Dietary Sodium on Urinary Sodium Excretion.—When patients entered the hospital having been on an unregulated diet, it was found that their sodium excretion usually ranged from 8 to 10 Gm. per twenty-four hours. When placed on bed rest and given a general hospital diet, their urinary sodium content dropped slightly during a three- to five-day interval and stabilized at 6 to 8 Gm. per twenty-four hours.

The effect of changes in the level of sodium intake was observed in one patient who was given 10 Gm. of salt daily in addition to her diet. It is apparent in Fig. 1 that there was a lag of three to five days before the sodium excretion reached the level of intake after the extra salt was given and again after it was discontinued. This exemplifies the need for maintaining a known sodium intake to evaluate the significance of changes in sodium excretion.

Effect of Forcing Fluids on Urinary Sodium.—It is customary in this clinic for all patients presenting evidence of toxemia of late pregnancy to be given a low salt diet and to receive fluids up to 4,000 c.c. daily. To check the effect of this schedule, normal pregnant women were placed on a similar regimen. In some patients, 6,000 c.c. of water were given orally in two to three hours to see if any augmentation in sodium excretion could be obtained. The effect of such fluid intake on sodium and urine excretion was noted and these data are illustrated in Fig. 2. It is apparent that urinary output can be increased by augmented fluid intake, but the excretion of sodium was decreased during the day of forced fluids. Not only was the concentration of sodium per liter of urine reduced, but the twenty-four-hour sodium output was also diminished. It made little difference whether the fluid was given in two to three hours or over the twenty-four-hour period. These findings are in accord with earlier reports that chloride excretion may be reduced by forcing fluids.

To check this effect 2,000 to 4,000 c.c. of fluids were given by vein. In these patients, there was also a slight decrease in urinary sodium concentration but the greatly increased urine volume produced a slight increase in the total sodium excreted in twenty-four hours, Fig. 3. There is a difference in the amount of sodium excreted whether the fluids are given by mouth or by vein.

The Effect of Intravenous Dextrose on Sodium Excretion.—To determine whether this apparent advantage of intravenous fluid in increasing sodium excretion was due to the dextrose or to the fluid, studies were undertaken to measure these factors. Two hundred grams of dextrose were given intravenously in 4,000 c.c. (5 per cent), in 2,000 c.c. (10 per cent), in 800 c.c. (25 per cent), or in 400 c.c. (50 per cent) (as rapidly as clinically feasible). The process was then reversed and the volume injected was held constant; the patients were given 400 c.c. of each solution, 5 per cent, 10 per cent, 25 per cent, or 50 per cent dextrose. The experimental day was measured from the onset of the infusion, usually from 8 A.M. to 8 A.M.

The twenty-four-hour urinary excretions obtained under these conditions are recorded in Figs. 3 and 4. When 200 Gm. of dextrose were given as 400 c.c. of a 50 per cent solution, there was usually a retention of sodium during the

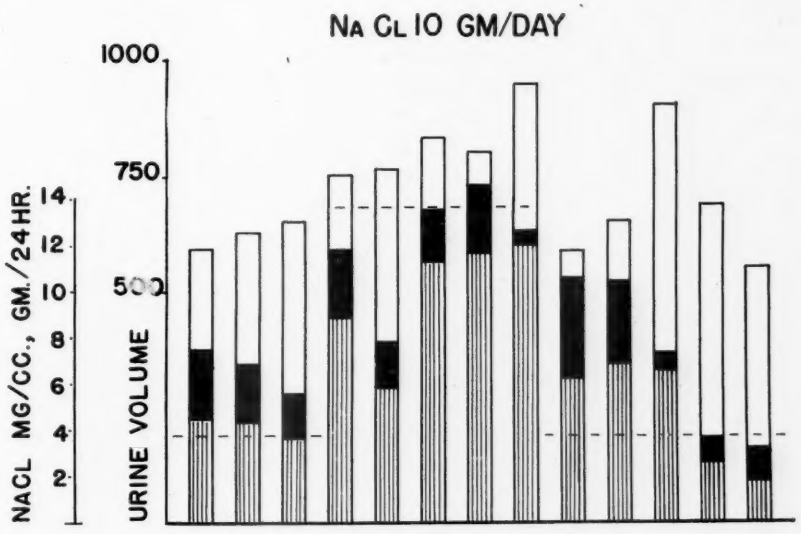


Fig. 1.—Graphic representation of the daily excretion of urine and sodium when the salt in the diet (3.8 Gm.) was augmented by giving an additional 10 Gm. a day for five days.

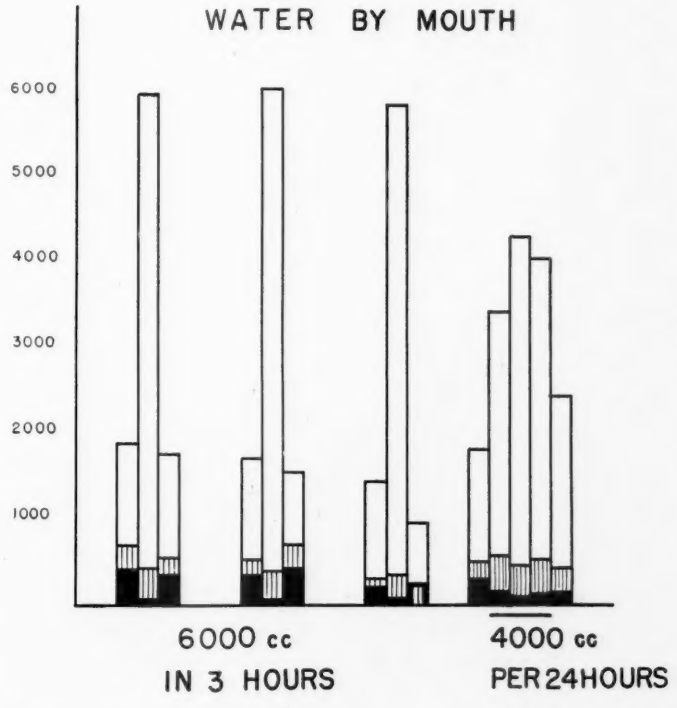


Fig. 2.—Graphic representation of the excretion of urine and sodium when fluids were given by mouth, 6,000 c.c. for one day, and 4,000 c.c. for three successive days.

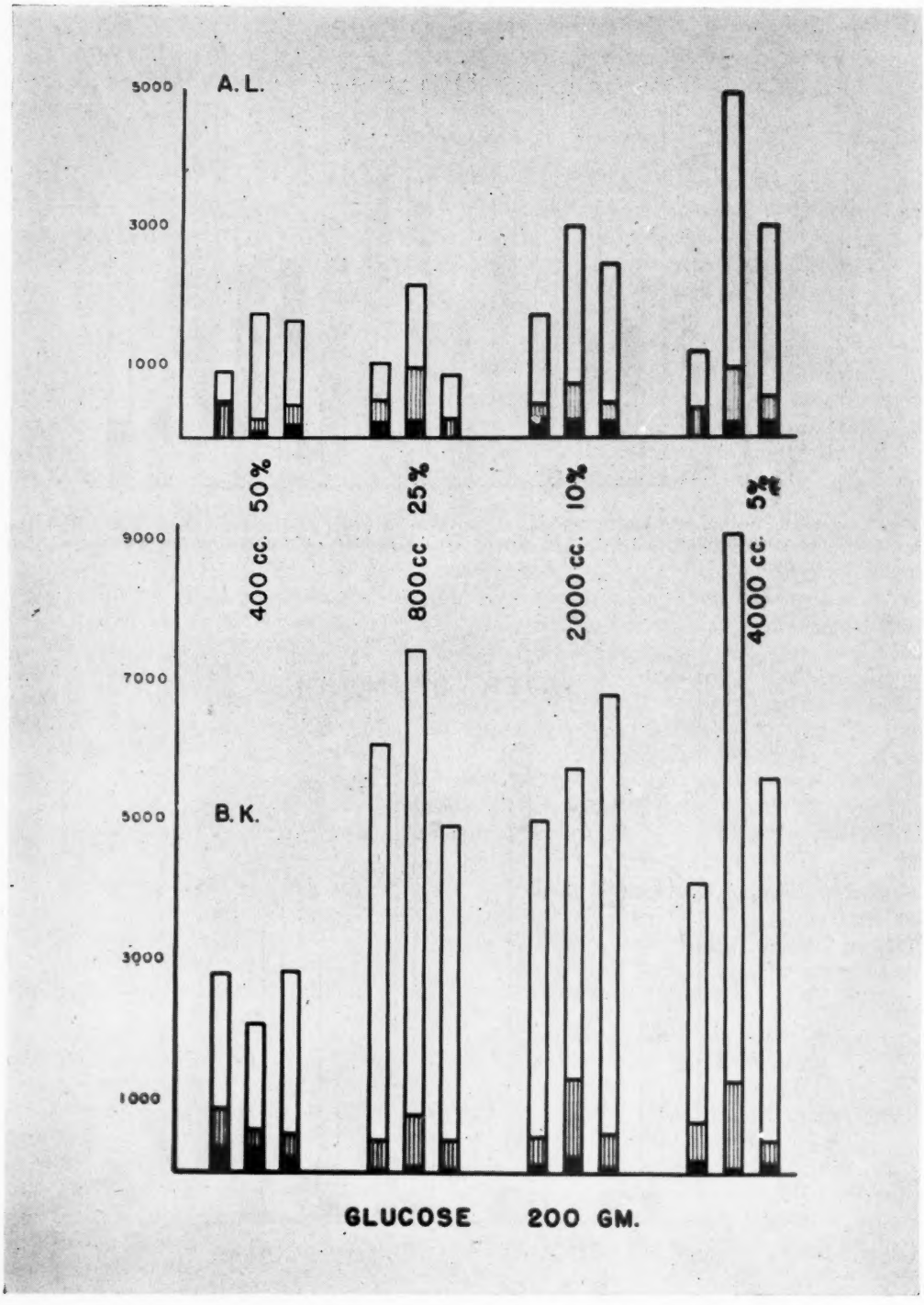


Fig. 3.—Graphic representation of the excretion of urine and sodium in two patients who were given intravenous solutions containing 200 Gm. of glucose (dextrose). The interval between these observations was five to seven days. The polydipsia and polyuria of B. K. lasted for about five weeks, but the effect of infusions of dextrose was still the same as in other patients.

twenty-four hours. As the volume of fluid was increased and the concentration of dextrose decreased, there was a progressive but slight increase in the twenty-four-hour sodium excretion so that the 200 Gm. of dextrose given as 4,000 c.c. of a 5 per cent solution produced a definite and consistent increase in sodium output. When the volume of injected dextrose was constant, there was no

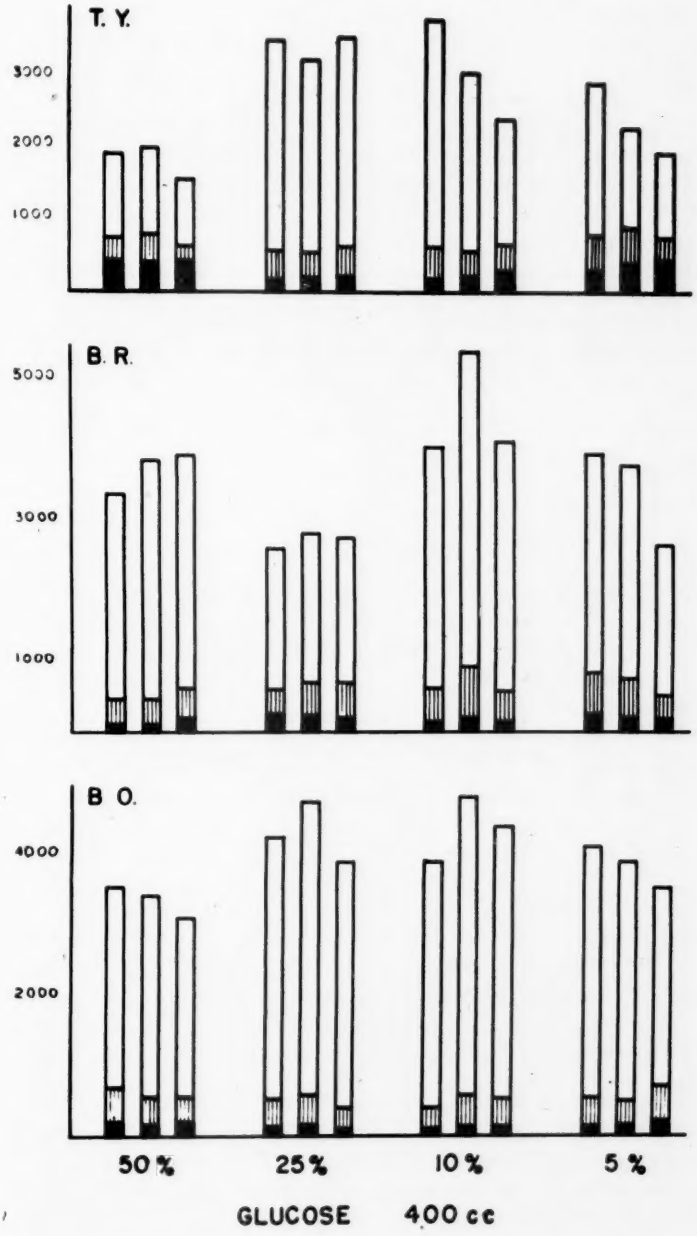


Fig. 4.—Graphic representation of the excretion of urine and sodium when patients were given 400 c.c. of glucose (dextrose) solutions intravenously. The interval between the injections in these three patients varied from five to seven days. There is no demonstrable effect on urine or sodium output even though the dose of dextrose varied from 20 to 200 Gm.

change in the urinary sodium output as the concentration of dextrose varied from 5 to 50 per cent. Thus it makes no difference whether 20 or 200 Gm. of dextrose is added to the 400 c.c. infusion when the total twenty-four-hour urinary volume or sodium is considered. Since any diuretic effect of a crystalloid is transitory, similar hourly fractional studies of sodium excretion were undertaken to ascertain whether an initial diuretic effect had been missed in the total twenty-four-hour sample. Eight hundred cubic centimeters seemed the maximal amount that could safely be introduced into the blood stream within two hours. The patients' schedules were arranged to provide urine samples at two-hour intervals from 8 A.M. to 8 P.M. Inlying urethral catheters were employed to insure that the bladder was emptied at the end of each two-hour interval. The overnight specimens were pooled. Urine samples were obtained in this manner for three successive days. Eight hundred cubic centimeters of 5 per cent or 25 per cent dextrose were given intravenously on the second day. (Fig. 5.) In each instance, there was a marked increase in urine during the period of infusion but in neither case did the urine output equal the amount of fluid injected. In the two-hour fractions, the sodium content and concentration were decreased but the twenty-four-hour output of sodium was not altered by either solution. The addition of dextrose to intravenous fluids does not seem to augment the diuretic effect of the water which carries it when measured by urine volume. This is found in both fractional and pooled twenty-four-hour specimens.

The administration of 800 c.c. of 25 per cent dextrose was followed by a diminished urine and sodium excretion (Fig. 5). The oliguric phase which follows the administration of a hypertonic solution has been shown to be due to the release of the antidiuretic hormone from the posterior pituitary.[4] This antidiuretic effect of hypertonic solutions detracts from their use as diuretic agents.

The Effect of Aminophylline on Sodium Excretion.—Aminophylline has not been extensively used in the treatment of edema of pregnancy, and very few data are available regarding its effect on sodium excretion. Most reports deal with the effect of aminophylline in conjunction with other diuretic agents and the effects are measured in terms of total urinary volume or of the decrease in weight of edematous patients. To study the effect of aminophylline alone as well as in conjunction with other agents, it was first given separately. A series of patients was given aminophylline intramuscularly in doses ranging from 1 grain b.i.d. to 7½ grains t.i.d. (120-1,500 mg. daily). The smaller doses of aminophylline had no measurable effect on the patient, the urinary volume, or on sodium excretion. When patients were given 7½ grains t.i.d. intramuscularly, vomiting occurred frequently. It is apparent that vomiting associated with aminophylline administration is central in origin. Despite this loss of sodium intake due to the vomitus, there was a marked increase in urinary sodium. This increase in urinary sodium was obtained primarily by an increase in sodium concentration in the urine. No evidence is available from these studies to explain the mechanism of the increase in sodium concentration in the urine (Fig. 6).

The Effect of Mercurials on Sodium Excretion.—Salyrgan was obtained without theophylline and injected intravenously into a series of patients at seven or eight o'clock in the morning in doses ranging from 2 to 4 c.c. (200 to 400 mg.). This mercurial caused a marked increase in urinary sodium and volume. This increase in sodium is due largely to an increased concentration in the urine (Fig. 7). The degree of increased sodium excretion varies with the dosage of mercurial administered. A dose of 2 c.c. was frequently ineffective

in increasing the urinary volume or total sodium excretion while 3 or 4 c.c. was consistently effective.

On the day following this marked output of sodium, there was a transient retention of sodium as manifested by a sharp drop in urinary sodium per twenty-four hours.

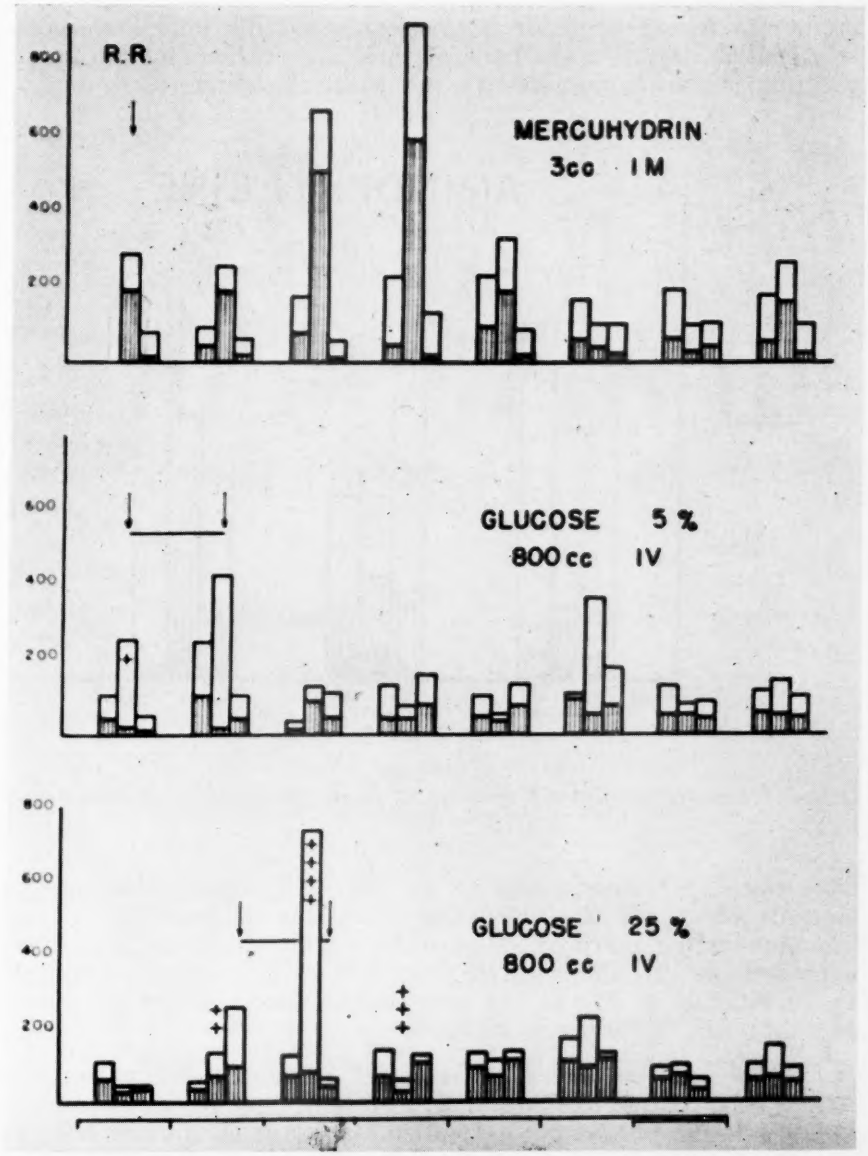


Fig. 5.—Graphic representation of the excretion of urine and sodium for two-hour intervals during the day when 5 per cent or 25 per cent glucose (dextrose) was given intravenously. The arrows indicate the duration of the infusion, about two hours. The overnight specimens were pooled and the two-hour average output is plotted over the wide bar in the base line. The total output for the twenty-four hours is also plotted as a two-hour average. The Mercuhydrin is included for contrast. Each 3-column group represents the same two-hour interval in the day on three successive days. The plus signs indicate glycosuria.

The Effect of Mercurial Theophylline Compounds on Sodium Excretion.—When theophylline is added to the mercurial compound (Salyrgan-theophylline or Mercuhydrin) an effect similar to that obtained with mercurials alone is observed. These data are recorded in Figs. 5 and 8. A considerable increase in urinary sodium excretion is obtained through the mechanism of increased sodium concentration and increased urinary volume.

The effect of Mercuhydrin appears within an hour and increases over a period of seven to eight hours (Fig. 5). In this case the amount of sodium excreted in the fourth two-hour interval exceeded the total excretion of the preceding control day. On the basis of these observations it appears that the mercurial compounds are most effective in mobilizing sodium.

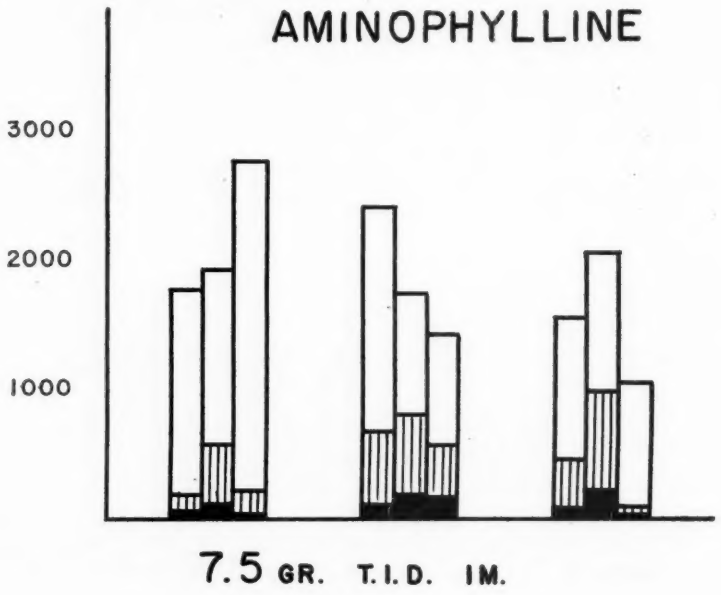


Fig. 6.—Graphic representation of the excretion of urine and sodium when aminophylline (7.5 grains t.i.d. – 1,500 mg.) was given intramuscularly.

The addition of theophylline to the mercurial agents does not increase their diuretic effect. It was noted that there was no vomiting in this series. Small non-nauseating doses of aminophylline were shown to be ineffective in mobilizing sodium. In all probability the lack of any additive effect obtained by this combination is due to the very small amount of the xanthine in the mercurial diuretics. (100 mg. to 200 mg.)

The Effect of Ammonium Chloride on Sodium Excretion.—Ammonium chloride has been the standard diuretic agent used in this clinic during the past years. It has been customary to give 8.0 Gm. daily in divided doses, and to continue it for four days. The effect of this regimen on mobilizing and excreting sodium and water was studied. In addition, some patients were given 12 and 16 Gm. of ammonium chloride daily, both orally and intravenously. The patients were on a standard diet containing 7.0 Gm. of sodium chloride a day. Eight grams of ammonium chloride caused a slight increase in sodium excretion, while 12.0 Gm. daily produced a significant increase in both urinary volume and sodium excretion per twenty-four hours. The sodium concentration, however,

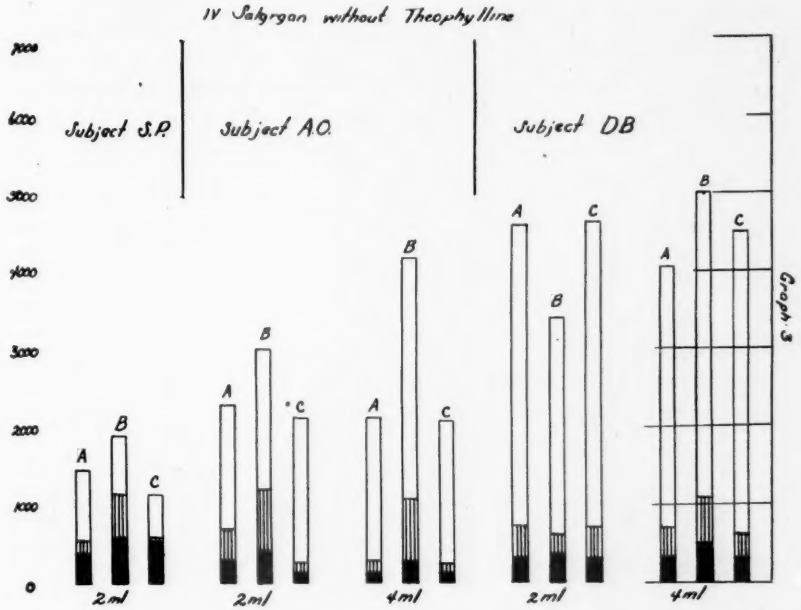


Fig. 7.—Graphic representation of the excretion of urine and sodium when salyrgan was administered in doses of 2 and 4 c.c. (ml).

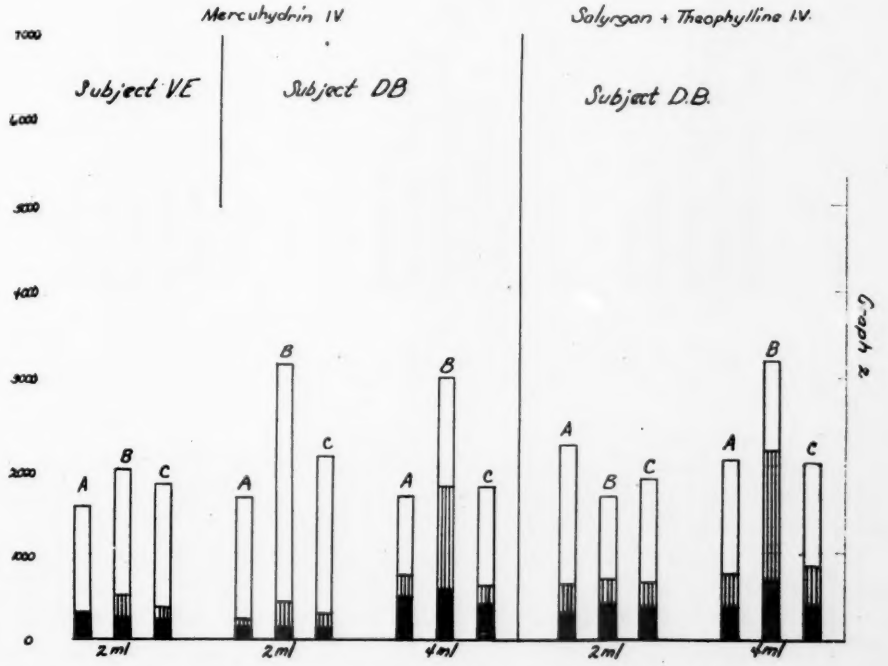


Fig. 8.—Graphic representation of the excretion of urine and sodium when mercuhydrin or salyrgan-theophylline was given in doses of 2 and 4 c.c. (ml) (mercurial 200-400 mg. with theophylline 100-200 mg.).

was not increased; the increased sodium output was due to increased urinary volume. Sixteen grams of ammonium chloride had an inconsistent effect probably because of interfering vomiting. Apparently there is no increase in sodium excretion over that due to the 12 Gm. dose, suggesting that that amount represents an optimal dose. It became apparent that the maximal effect was obtained within twenty-four to forty-eight hours and that continued treatment had no

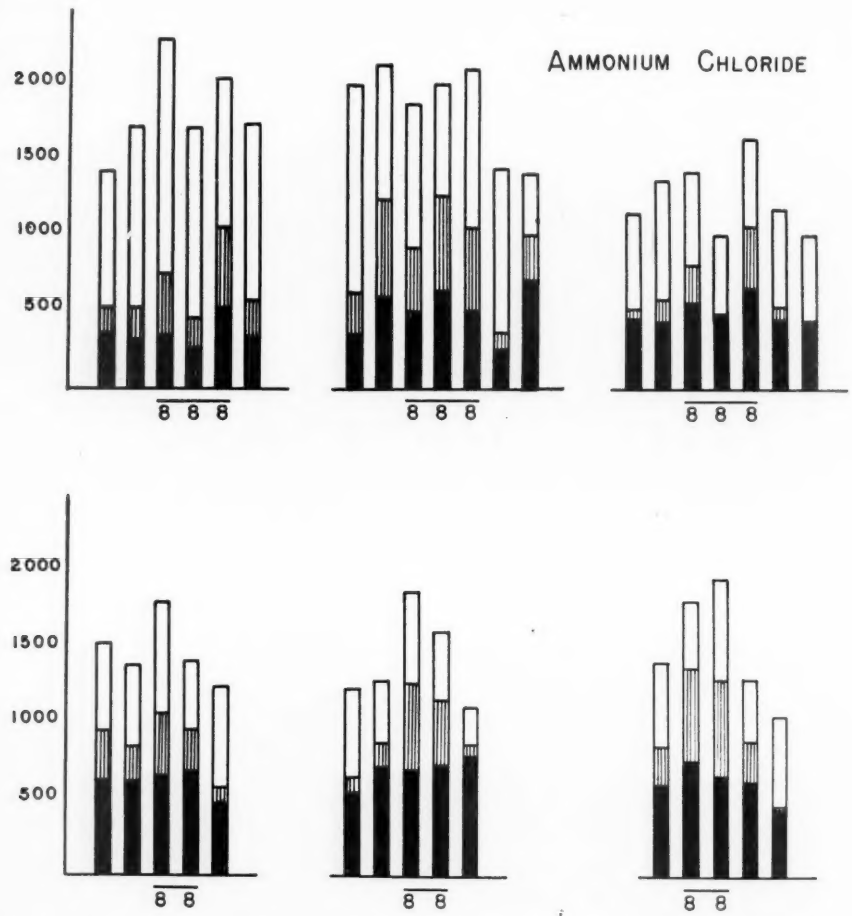


Fig. 9.—Graphic representation of the excretion of urine and sodium when 8 Gm. of ammonium chloride and given for three days (upper row of three patients) and given for two days (lower row).

effect on urinary sodium excretion or urinary volume. A decrease in sodium excretion occurred in some patients during the continued administration of ammonium chloride (Figs. 9 and 10).

When the dietary sodium was decreased to 2.0 Gm. per twenty-four hours, ammonium chloride had no effect on urinary sodium output Apparently there must be a fair supply of available sodium for its increased excretion to be obtained with ammonium chloride.

It has been suggested that the ammonium chloride produces its effect through the following mechanisms: The ammonium ion is combined with carbon dioxide in the liver to produce urea. The urea is a neutral substance

and is excreted as such. The negative chloride ions produce a state of acidosis which is reduced by a reaction of the excess chloride ions with the sodium bicarbonate buffer to form sodium chloride and carbon dioxide. Sodium chloride is excreted in the urine and carries with it an increased volume of water; the carbon dioxide is eliminated through the lungs and further reduces the acidosis.

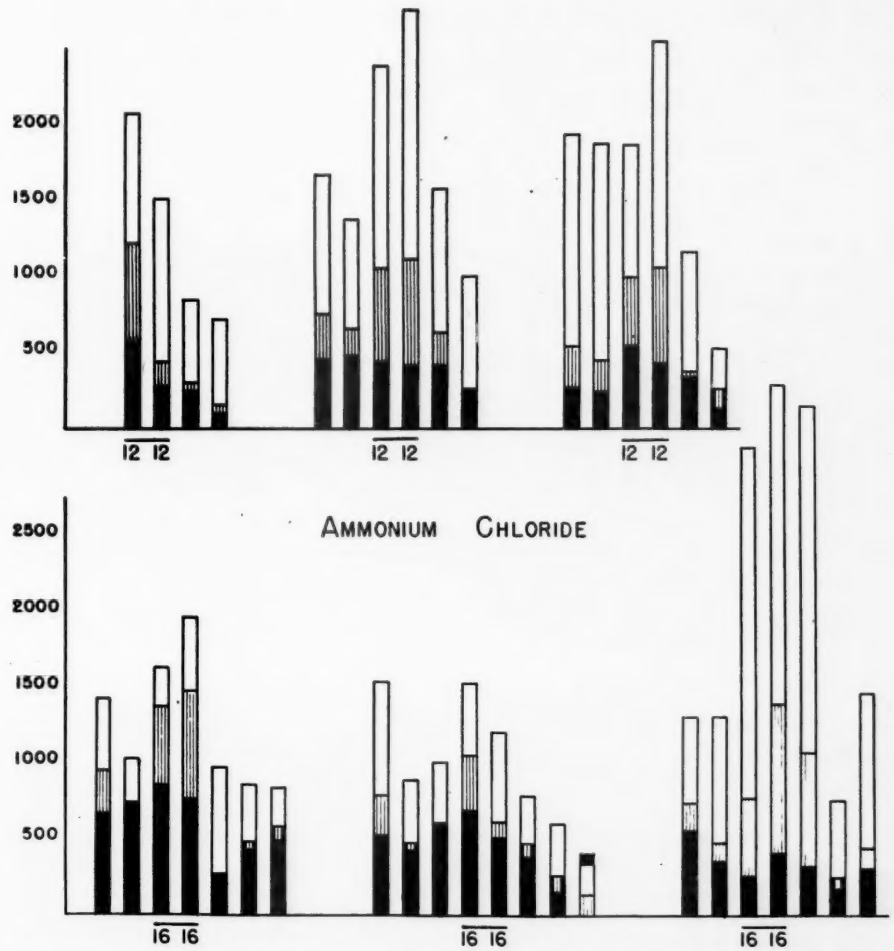


Fig. 10.—Graphic representation of the excretion of urine and sodium when 12 or 16 Gm. of ammonium chloride was given for two days.

The validity of this theory was tested by measuring urinary sodium, chloride, ammonia, urine volume, and blood carbon dioxide combining power. The results are tabulated in Fig. 11. This concept seems to be basically correct for there was an increased urinary sodium and urea associated with the increased urinary volume. There was also an increase in chloride more than could be accounted for by the increased urinary sodium. The absence of an increase in urinary ammonia indicates that little if any ammonium chloride is excreted. The excess chlorides found in the urine were in combination with some undetermined cation. In these patients the increase in sodium excretion was associated with a drop in carbon dioxide combining power, which indicates a loss of buffer sodium salts.

In a prior study observations on weight loss and changes in blood carbon dioxide combining power were recorded during the intravenous injection of ammonium chloride.

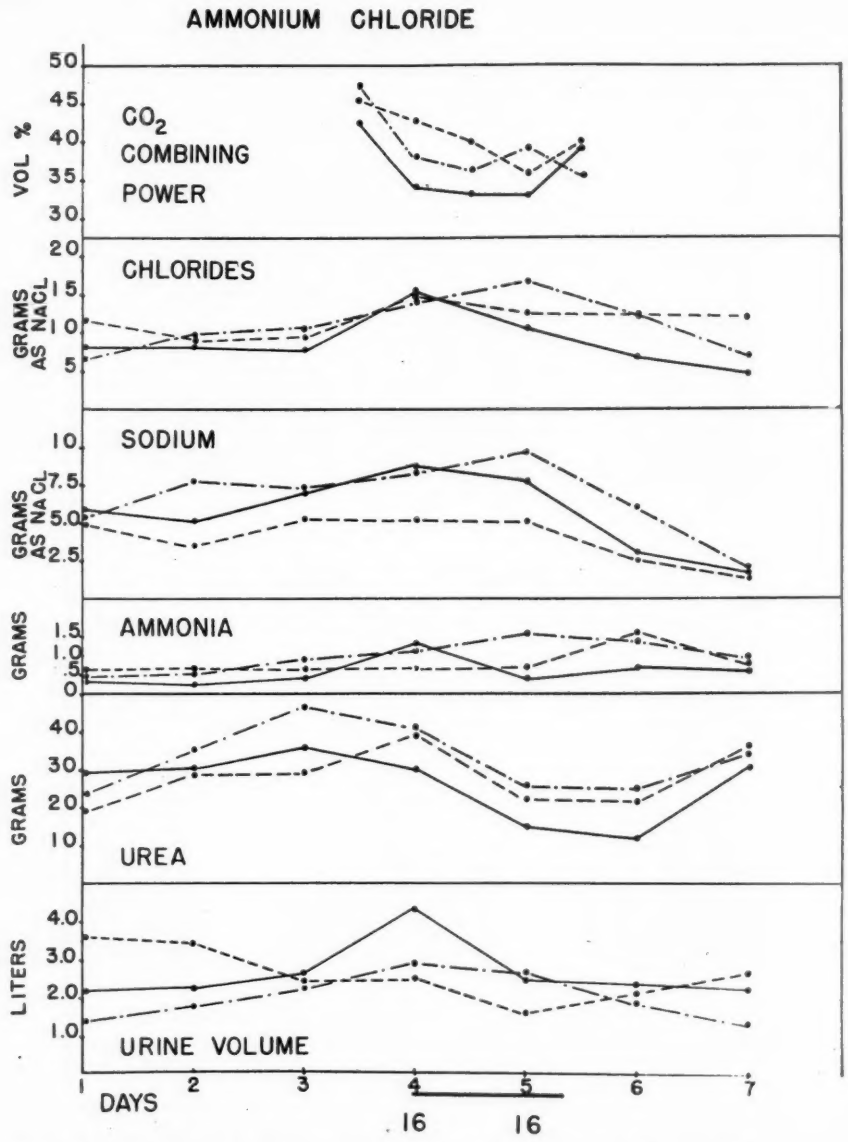


Fig. 11.—Variations in urinary constituents and blood carbon dioxide combining power when 16 Gm. of ammonium chloride was given to three patients.

Ammonium chloride was prepared as chemically pure crystals and autoclaved in ampules. It was determined that from 0.5 to 1 per cent ammonium chloride in 5 per cent dextrose would not produce hemolysis in vitro and was a satisfactory solution for intravenous injection. When 10 to 15 Gm. of ammonium chloride were injected into patients, vomiting occasionally occurred. Rapid injection seemed to favor vomiting. This suggests that the vomiting associated with ammonium chloride administration may be central in origin.

It was observed that effective mobilization of edema occurred over a short period of time and was associated with a considerable decrease in the blood carbon dioxide combining power. (Fig. 12.) Prompt weight loss can be induced by the intravenous injection of ammonium chloride and the resulting acidosis.

It thus appears that ammonium chloride administration can increase urinary sodium excretion, that this increase is of short duration, and may not be maintained even with the continued administration of the drug. The increase in sodium excretion is effected by an increase in urinary volume rather than by increased sodium concentration. Twelve grams of ammonium chloride seems to be a satisfactory daily dose.

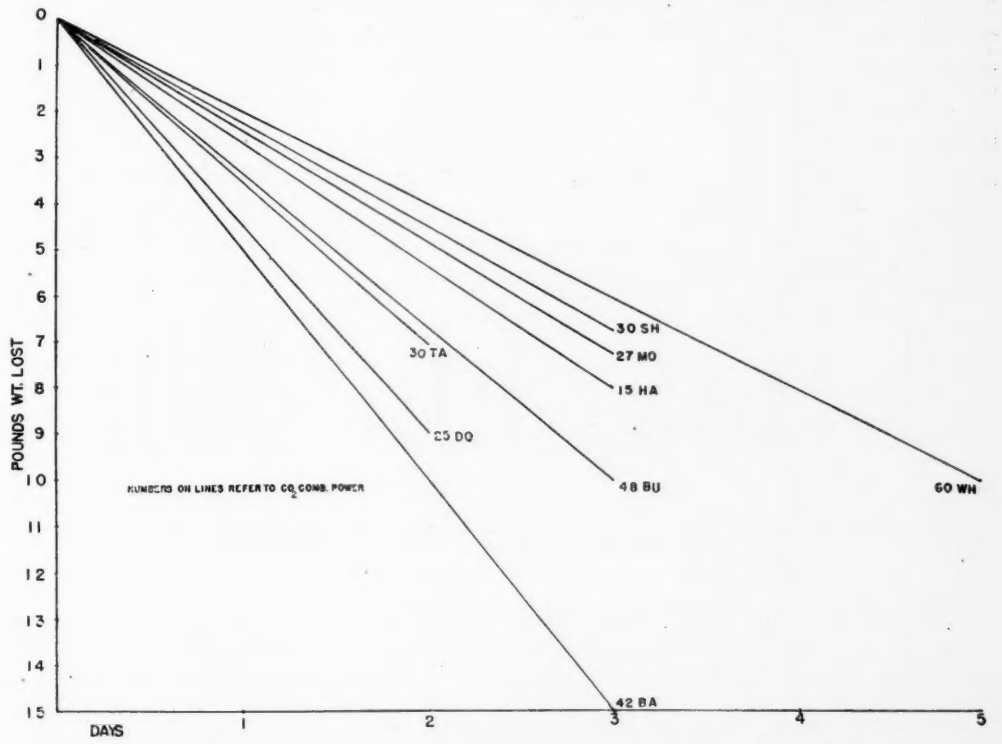


Fig. 12.—Graph showing weight loss in eight toxemic patients given 10 to 15 Gm. per day of ammonium chloride intravenously in 5 per cent dextrose. The figures represent carbon dioxdide combining power and the patients' initials.

The Effect of Urea on Sodium Excretion.—It has been suggested that urea is a diuretic agent that operates by increasing urinary volume. In order to determine the effect of urea, patients were given 60 Gm. of urea daily. The data from these studies are recorded in Fig. 13. There is a questionable transitory increase in urinary volume, which may be due to the considerable volume of fluid necessary to ingest the urea. There was no increase in urinary sodium and no alteration in sodium concentration in the urine.

Sodium and Water Excretion in Toxemic Pregnancies.—It is apparent from the above data that certain agents are more effective in the mobilization and excretion of sodium than are others. Since these studies were carried out on

normal pregnant patients it was of interest to determine whether a similar mechanism was operative in patients with toxemia of late pregnancy. Three patients with moderately severe toxemia were studied with regard to both sodium and urinary excretion. They were placed on the usual routine of low sodium diet, liberal fluids by mouth, 8.0 Gm. of ammonium chloride daily, and bed rest. After stabilization on this schedule, they were given intravenous dextrose; there was a slight increase in urinary volume but no increase in a twenty-four-hour sodium output. Two cubic centimeters of Mercuhydrin were then given and it produced both a marked diuretic and sodium excretion effect. This suggests that toxemic patients respond similarly to normal pregnant women as regards the dextrose and mercurial diuretics.

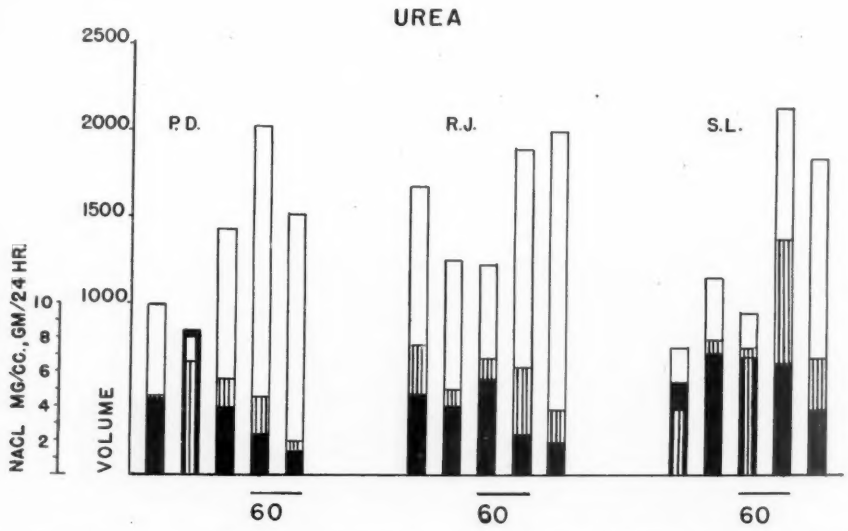


Fig. 13.—Graphic representation of the excretion of urine and sodium for three nonpregnant subjects receiving 60 Gm. of urea on two successive days.

The patients reported under the section on intravenous ammonium chloride (Fig. 12) all had toxemia and showed a very satisfactory weight loss indirectly indicating loss of water and sodium. Three eclamptic patients who had progressed to the point of marked oliguria (10 c.c. per hour or less) or complete anuria were given varying concentrations of glucose by vein without effect. Seven and one-half grains of aminophylline were given intramuscularly and in two of the three patients urinary flow was established within a few hours. These urines contained high concentrations of sodium. This suggests that anuric and oliguric patients may respond to aminophylline in a similar manner to normal pregnant women.

Sufficient studies have not been made on toxemic women to indicate the effectiveness of these agents in the clinical management of the disease. These notations are included because they suggest that the mechanism of sodium excretion is of a similar nature in normal and toxemic pregnancies.

An attempt was made to test the suggestions that morphine might have an antidiuretic effect. Twenty patients were given variable amounts of 5 per cent dextrose intravenously at a constant rate each day. On alternate days they were given 10 to 15 mg. of morphine at the onset of the infusion. Many but not all of these patients showed a sodium and water retention for three or four

hours. If these observations are confirmed, they suggest that the large doses of morphine commonly used in the control of eclampsia may contribute to an oliguria or anuria.

Discussion

From the experimental data, it becomes apparent that sodium excretion is a complex process and that a variety of factors modify its mobilization. From the standpoint of clinical management of toxemic patients, no evidence is presented as to the relative value of increasing urinary volume or urinary sodium excretion. These studies do not offer any evidence on the basic abnormality productive of edema, namely, whether it is a disorder of sodium or water metabolism. The effect of diuretic agents on twenty-four-hour urinary volume and sodium excretion is relatively transitory. Except in the case of ammonium chloride, no attempt has been made to introduce these agents continuously. As far as the mercurials were concerned, this was avoided both because of concern about potential renal damage to the women and because of statements in the literature that the effect would last for several days. The data obtained in these experiments suggest that the effect on sodium excretion is relatively transitory, lasting about twenty-four hours. In the case of ammonium chloride even the continued administration of the drug is not attended by maintenance of increased urine or sodium excretion.

In practically every case following excessive sodium mobilization, there was a transitory (probably compensatory) retention of sodium apparently to permit a restoration of sodium balance. Sodium retention was especially marked the day after the use of mercurials or large doses of aminophylline. It is interesting to note that with hypertonic glucose there is a transitory increase in urine volume apparent only when hourly fractionated studies were run. However, even during the diuretic phase the amount of fluid eliminated is not as great as that injected and then a period of oliguria and decreased sodium excretion follows within two hours.

It became apparent that the so-called diuretic agents have been very loosely defined. When one introduces 1,000 c.c. of fluid into the blood stream and recovers 800 c.c. of urine, it becomes a question as to whether or not the fluid represents a diuretic. Hourly urine collections show an apparent increase in urinary volume over and above the control period. If this increase in urine output is less than the normal excretion plus the increment introduced by vein, it becomes a matter of opinion as to whether the increase in urine is a straight filtration phenomenon produced by the fluid introduced, or whether it represents a diuretic effect. Since the total output is less than the total intake (whether measured on an hourly or on a twenty-four-hour basis) these studies suggest that hypertonic solutions of crystalloids introduced into the blood stream are ineffective as diuretics. However, by contrast, the introduction of 3 to 4 c.c. of a mercurial diuretic will cause a marked increase in urinary volume in which the fluid volume of the injected material becomes negligible. It would seem that

the latter type of agent might be rightfully called a diuretic. This group includes the mercurial and xanthine compounds. It is of interest in this connection to consider the effect of intramuscular aminophylline in large doses. Despite a decreased intake of fluid and sodium induced by vomiting, there may be increase in urinary volume. Thus it becomes apparent that aminophylline is a diuretic agent in that it can mobilize and excrete fluid and sodium even in the face of decreased intake.

It is of interest to note that some preparations which are popular as diuretics such as urea and dextrose were shown to be ineffective in that they did not increase urine output.

There seems to be a slight increase in urine volume and sodium excretion induced by adequate amounts of ammonium chloride. It is of interest to note that this effect of ammonium chloride is almost entirely eliminated by the sharp reduction in dietary sodium. Explanation of this phenomenon is not apparent. It would appear that the effect of the shift in the acid base balance, which necessitates the mobilization of sodium and other buffer salts, takes place only in the presence of available sodium. Moreover, the continued administration of ammonium chloride over the second and third day, after an increased sodium excretion has been obtained, is relatively ineffective.

The increase in urinary volume associated with ammonium chloride administration is difficult to evaluate. The patients who received the 12 and 16 grams of ammonium chloride became thirsty and ingested a larger volume of water. The increase of urinary output, therefore, may simply represent a function of the increased ingestion of fluid rather than any direct diuretic effect of ammonium chloride.

When one studies the effects of these diuretic agents on sodium excretion, their action tends to fall into three general categories. In the first place increased urinary sodium output can be induced in patients by giving fluid by vein. While this effect is slight, it is apparent when hypotonic solutions are given in a relatively short period of time. The increased urinary sodium excretion is obtained with a decreased sodium concentration in an increased output. This type of effect we have called a "wash out" mechanism. It appears that the increased urinary sodium is obtained by the direct effect of an augmented urinary volume produced by the increased fluid intake.

A second mechanism of increased sodium excretion is produced by a change in acid base balance. Ammonium chloride is the best example of this type. An increase in urinary sodium can be obtained if one produces a rather rapid and sudden shift toward the acid side. Apparently this change mobilizes sodium to compensate for a relative acidosis, and thus an increased amount of sodium is excreted by the kidneys.* This increased sodium excretion is brought about by

*While most authorities suggest that the diuretic effect of aminophylline is due to a change in glomerular filtration it is of interest to note that the clinical picture of nausea, dizziness, vomiting, and thirst which are apparent with ammonium chloride medication, is likewise apparent in the large effective doses of aminophylline.

an increase in urinary volume but without change in sodium concentration. This is in contrast to the decreased sodium concentration found in patients described under the "wash-out" process discussed above.

The third mechanism by which sodium excretion may be increased is through some change in renal function. Mercurial and xanthine diuretics produce this type of effect. They cause a moderate increase in urinary volume and the most marked increase in total urinary sodium of any of the agents studied. This effect can be obtained with either the mercurials or aminophylline but, from the pharmacological point of view, there seems to be little advantage in combining the two as in the commercial compounds. Because of the small amounts of aminophylline in the pharmaceutical preparations, it is impossible to judge the additive effect produced by the combination. It would be of interest to learn whether an increased amount of aminophylline together with a mercurial diuretic would cause an augmented effect.

While the studies which are available on toxemic patients are too few to be of any clinical value, it is of interest that apparently the toxemic patient handles water and sodium in a manner similar to the normal pregnant woman and will respond in a similar fashion to diuretic agents. The evidence available suggests that the mercurials and xanthines are worthy of clinical trial in the management of toxemic patients.

The clinical management of toxemic patients generally includes a liberal use of sedatives, such as morphine. If the observations of the antidiuretic effect of morphine are confirmed, its use in patients with oliguria may need to be restricted.

As yet there is no good explanation why the toxemic patients who excrete large volumes of urine and are losing weight have a better prognosis than those patients who do not respond. Nevertheless, there is general clinical agreement that such is the case. It would appear, therefore, that, on the basis of these experimental observations, toxemic patients might be improved by the clinical trial of some of these preparations. In all probability, the edema is not the cause of toxemia of pregnancy but is merely a symptom of an underlying biochemical derangement which has not yet been identified.

Conclusions

1. Diuretic agents vary in their ability to increase the excretion of water and/or sodium.

2. Diuretic agents increase sodium excretion by three mechanisms: (a) by a "wash-out" process induced by increased fluids given intravenously; (b) by the production of an acidosis; (c) by a change in renal function which increases the concentration of sodium in the urine.

3. Hypertonic dextrose solutions do not increase sodium or water excretion.

4. Induced increases in sodium excretion are transitory (twenty-four to forty-eight hours).

5. Apparently toxemic and normal pregnant women respond similarly to diuretic agents.

We are indebted to Donna MacLachlan, Betty Jean Harpley, and Erlene Peterson for the dietary management and for the sodium determinations on the patients used in this study.

Addendum

Since submitting this manuscript for publication, we have given hypertonic dextrose intravenously at a more rapid rate in four instances. Normal women were given 800 c.c. of 25 per cent dextrose at a rate of 0.25 c.c. per kg. (approximately 16 c.c.) per minute. During the forty-five to fifty minutes of the infusion, the output of urine increased when the blood sugar concentration exceeded 500 mg. per cent and the urine sugar concentration was over 1 per cent. However, the increase in urine flow over that of the control interval was less than 16 c.c. per minute so that not all of the infused fluid was recovered. In only one fifteen-minute interval, in one patient, did the increase in urine flow equal or exceed the 16 c.c. per minute increment which was given as 25 per cent dextrose. In two instances the urine output decreased during the last fifteen minutes of the infusion. Immediately after the discontinuance of the intravenous dextrose, the urine flow diminished rapidly as the blood sugar levels dropped.

The abrupt decrease in urine flow after the administration of hypertonic solution was discontinued, and its decrease during the infusion in two instances, suggested that the increased osmotic pressure of the blood may have caused the liberation of antidiuretic hormone from the posterior pituitary. This response of the neurohypophysis would tend to defeat the purpose of the hypertonic intravenous fluid.[4, 5, 6] Even though the urine output was increased during the rapid infusion of dextrose, in our experience, this increment of urine was not apparent in a total twenty-four-hour urine volume and was less than the amount of extra fluid administered.

References

1. Davis, A. K., and Overman, R. R.: Federation Proc. Part II, 6: 94, 1947.
2. Barber, H. H., and Kohltoff, I. M.: J. Am. Chem. Soc. 50: 1625, 1928.
3. Bradbury, J. T.: J. Lab. & Clin. Med. 31: 1257, 1946.
4. Chambers, G. H., Melville, E. V., Hare, R. S., and Hare, K.: Am. J. Physiol. 144: 311, 1945.
5. Carter and Robbins: J. Clin. Endocrinol. 7: 753, 1947.
6. Verney: Proc. Roy. Soc. London s.B. 135: 25, 1947.

Discussion

DR. FRANK E. WHITACRE, Memphis, Tenn.—Drs. Brown and Bradbury have brought out so many factors in this timely report that any one of them could be the subject of debate among the physiologists, pathologists, and clinicians. In reviewing this extensive piece of work, water balance is of special interest.

Dextrose, from this report, is no better as a diuretic than water. It would be helpful to know more accurately the speed of administration of hypertonic dextrose solution, as it is well known that this has considerable effect upon the volume of urine returned, and, to expect a diuretic effect, the renal threshold must be exceeded. Some of the water is retained with glucose as the glucose is rapidly absorbed from the blood. Any procedure which attempts to increase sodium excretion will be followed by a period of sodium retention until the balance is restored. Sodium and water are presumably retained in the body by some extra renal mechanism. One can reduce water and sodium temporarily, but after the diuretic procedure is stopped, both are retained as before. Sodium and water retained in edema fluid are inaccessible to the kidney unless some diuretic agent is used. Water excretion reflects primary reciprocal changes in tubular reabsorption of water. Daily variations in water excretion are believed to be due to changes in facultative water reabsorption through the antidiuretic

hormone mechanism. It is possible that this mechanism is involved in the disturbances of our toxemic patients. The amount of sodium and chloride reabsorbed varies inversely with the A. D. H. concentration, but the amount of water reabsorbed varies directly.

The combination of ammonium chloride and dextrose seems to be innocuous treatment and caused considerable weight loss through the excretion of water and salt. However, if used for very long, acidosis could result due to depletion of alkali reserve.

The effect of mercurial diuretics is that they block the tubular absorption of sodium and chloride. They have been considered to be ideal diuretics and widely used, and the suggestion of the authors that they be given a try in toxemic patients must be carefully considered. There is evidence that the mercurials can cause necrosis of the convoluted tubules leading to irreparable damage. Sprunt has reported that in 741 autopsies, nine had received mercurial diuretics and of these, three showed necrosis of the tubular epithelium. He could not correlate the amount given with the extent of the renal damage (Arch. Int. Med. 46: 494, Sept. 1930). It seems reasonable to conclude that where contraindications, such as fever, tuberculosis, or chronic nephritis are present or, if there is evidence of kidney damage, the mercurial diuretics should not be used.

The effects of the various diuretic agents mentioned should not be left without emphasizing another factor. Generalized angiospasm in the toxemic patient could be expected to reduce renal blood flow, and the effect of diuretic agents is enhanced by relieving by various commonly applied means the spasticity of the arterioles.

It is a good thing for someone to bring into question our established ideas on what a diuretic really is, and it is questionable that a substance can be considered as a diuretic when the amount of fluid given to the patient so far exceeds the amount returned in the urine.

DR. LESTER ODELL, Chicago.—During the past six months at the Chicago Lying-in Hospital the effect of the various diuretics has been reinvestigated. Our efforts have been directed toward urine sodium and the volume of urine excreted. Employing the diuretic agents recommended by Dr. Brown, we found more sodium excreted and a greater urinary volume following hypertonic glucose. We feel that the urinary volume is the best single prognostic guide we have in eclampsia. We have advocated the use of intravenous hypertonic glucose in maintaining an adequate urinary volume, and recommend 1,000 ml. of 20 per cent glucose every eight hours. If such concentrations are unsuccessful, use 750 ml. of 30 per cent or 400 ml. of 50 per cent glucose solutions. Hypertonic glucose is the best thing available at present for maintaining the adequate urine volume so necessary for recovery of the eclamptic patient.

I would like to ask Dr. Brown two questions: First, how many severe toxemias of pregnancy have been treated by mercurial diuretics alone? And by the term "diuretic" I mean to include hypertonic glucose solutions. Secondly, in using mercurial diuretics clinically, how can one be sure that no renal disease exists? In short, how will one differentiate between severe preeclampsia and nephritis prior to the use of mercury?

DR. BROWN (Closing).—We wish to point out that this report was designed to make available basic information about the action of these diuretic agents in excreting sodium. We have presented no evidence that sodium or water retention has necessarily anything to do with the outcome of toxemia of pregnancy. It is generally agreed that if an increased urinary volume is obtained, these patients are improved. These observations offer mechanisms by which increased urinary sodium and volume can be accomplished. It is yet to be proved that these changes have a beneficial clinical effect.

The question of what constitutes a diuretic has to be considered. According to our interpretation, if one administers 1,000 c.c. of solution to a patient and recovers only 500 to 800 c.c. in the urine, that agent is not a diuretic. I do not disagree that the patients at the Chicago Lying-In Hospital are improved, but I do question that intravenous hypertonic glucose solution is a diuretic agent.

In answer to Dr. Whitacre's question, I would like to show three slides. The first slide demonstrates the similar effect produced by giving 6,000 c.c. of water in three hours and in

twenty-four hours (Fig. 2). The second slide compares the effect of intravenous glucose (isotonic and hypertonic) given in two hours (Fig. 5) and over six hours (Fig. 3). The rate of administration in these experiments had no apparent effect on the twenty-four-hour urinary volume or sodium output.

From these studies it is apparent that sodium and water excretion can be manipulated independently of each other. Increased urine volume may be obtained with both high and low concentration of sodium. Likewise, the amount of sodium in the urine can be increased with minimal increase in urine volumes.

In presenting this material, we hope others will be encouraged to try these agents in the clinical management of toxemia so that we may come to learn their true value. We now have a method for studying both sodium and water excretion independently of each other.

MESONEPHRIC REMNANTS IN THE CERVIX*

JOHN W. HUFFMAN, M.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology, Northwestern University Medical School)

IT IS well known that certain portions of the mesonephros may persist near the ovary and in the broad ligament and the vagina of the adult human female. That fetal remnants of mesonephric origin may persist in the uterine cervix is less commonly realized. From time to time reports have appeared in the European literature commenting on the development of tumors arising from mesonephric residues in the cervix. Meyer[1-3] has presented factual data establishing the embryonic source of such neoplasms as being from the cervical portion of the mesonephric duct.

With the exception of Wolfe's case reports several years ago,[4] the American literature has contained no reference to this unique and unusual problem. It should be a matter of interest shared in common by the clinician, the gynecologic histopathologist, and the embryologist. This is particularly true when it is realized that mesonephric remnants in the cervix may cause confusion in the histologic study of surgically excised tissues and that they may give rise to bizarre tumors which can be either benign or malignant. Because of the paucity and the relative inaccessibility of available information on the subject, it has seemed worth while to make this presentation an attempt to portray in definitive fashion the embryology, the histology, and the microscopic pathology of mesonephric remnants in the uterine cervix. In order to accomplish this the literature has been reviewed, serially sectioned tissues have been studied, and sections from 1,192 surgically excised cervices in the gynecologic laboratory at Northwestern University Medical School (comprising tissues from Passavant Memorial and Wesley Memorial Hospitals) have been examined.

In the development of the female urogenital system it will be recalled that the first primitive organ is the pronephros and that as a result of fusion of the pronephric tubules a pair of collecting ducts develop. After the degeneration of the pronephros the two excretory ducts persist as the mesonephric (wolffian) ducts into which the mesonephric tubules empty (Fig. 1). These ducts extend caudally along each side of the celomic cavity to empty into the ventrolateral portions of the cloaca. The paired paramesonephric (müllerian) ducts extend first lateral and then medial to the mesonephric ducts. As the mesonephric and paramesonephric ducts increase in size, a fold of peritoneum (the urogenital fold) grows about them. The caudal portions of these two lateral urogenital folds fuse transversely in the lower abdomen to form a medially placed genital cord. In the center of this genital cord are the two paramesonephric ducts

*Read by invitation, before the Central Association of Obstetricians and Gynecologists, Oct. 25, 1947, Louisville, Ky.

(müllerian) which later fuse to form the uterovaginal canal. Somewhat lateral to the paramesonephric ducts but still within the genital cord are the paired mesonephric ducts.

From the 4 to the 55 mm. stage of embryonic development the mesonephric ducts empty into the cloaca and later the urogenital sinus. During this period they lie in the genital cord parallel and lateral to the paramesonephric ducts and are intact throughout their lengths (Fig. 2). Shortly after the 55 mm. stage, however, the openings in the urogenital sinus close and degeneration of the mesonephric ducts begins (Fig. 3). This degeneration continues throughout the remainder of embryonic life and in most individuals only a few vestiges of the mesonephric tissues persist: in the adult degenerated portions may be found near the ovary, in the mesosalpinx, and in the broad ligament. Occasionally persistent portions of the mesonephric ducts become dilated in the anterolateral or lateral vaginal walls to form the familiar Gartner's duct cysts.

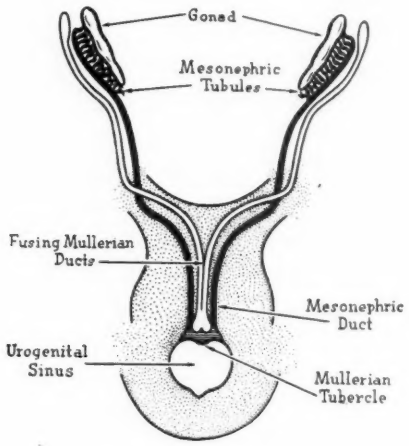


Fig. 1.—Diagram of the urogenital system at an early stage in fetal development. The mesonephric ducts extend caudally along each side of the fusing paramesonephric ducts within the genital cord.

While the sequence of events in the development and degeneration of the mesonephric tissues as just described applies to the majority of individuals, Meyer has demonstrated that certain interesting exceptions may occur. Meyer[5] has shown that an ampullar dilated portion of the mesonephric duct is frequently observed as a rather wide circular enlargement of the duct lumen in the fetus as early as the second month. In older embryos the mesonephric duct is occasionally found as a narrow cylindrical tube penetrating from the parametrium into the middle of the lateral uterine wall. From this point of entrance the duct proceeds in a downward direction in the uterine wall (Fig. 4). As it enters the lowermost corpus and cervix the narrow cylindrical lumen dilates to form a distended ampulla located in the middle muscle layers of the lateral cervical walls. At the end of the fifth month of fetal life the ampulla forms a cleftlike cavity which has, in cross section, slight bends and curves and the beginnings of a few rather large diverticula (Fig. 5).

When the mesonephric duct persists in the cervix (in approximately 20 per cent of the fetuses Meyer[6] examined), it reaches its full development at the seventh or eighth month of fetal life. At this time the ampulla lies chiefly in the lower part of the supravaginal portion of the cervix and in the upper portion

of the portio vaginalis. The dilated ampulla extends downward from the upper cervix as an elongated dorsoventral slit lying in the middle muscle layers of the lateral cervical walls. From the portio vaginalis the duct turns and runs laterally in a diagonal upward direction until it passes over into the vagina.

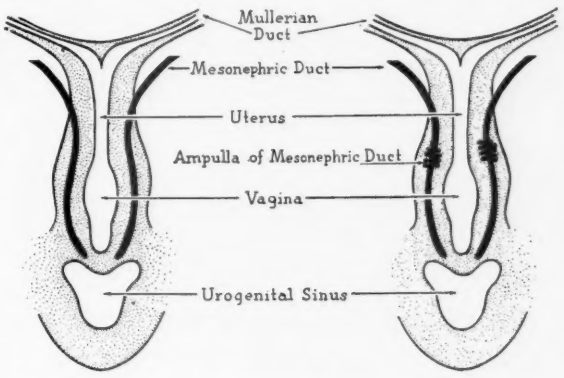


Fig. 2.—Diagram. Prior to their degeneration the mesonephric ducts extend along each side of the uterovaginal canal (which was formed by the fusion of the paramesonephric ducts, *A*. Mesonephric ampullae tubular diverticula develop in some (20 per cent according to Meyer) fetal uteri, *B*.

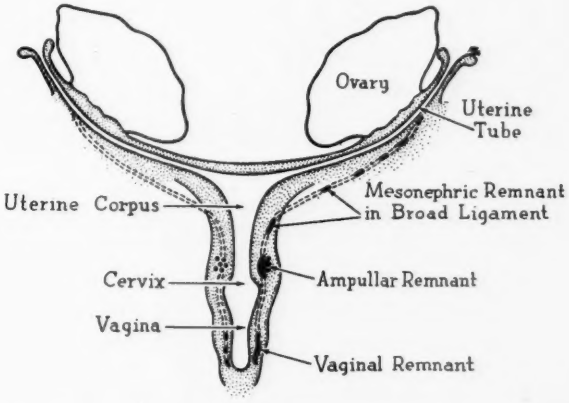


Fig. 3.—Diagram. Degeneration of the mesonephric duct begins during the later stages of fetal development. This degeneration may be complete or remnants may be left in the vaginal wall, the cervix, the uterine wall, or the broad ligament or near the ovary.

At the point where the ampulla turns laterally in the cervix it sends more or less deep branches into the substance of the cervix. These branches may form extensive coiled or snarled twisted canaliculi or tubules which extend into the anterior and posterior portions of the cervix. After the duct passes over into the vagina it again becomes narrower and assumes a cylindrical tubular form as it extends downward along the anterolateral vaginal wall to terminate near the hymen.

In the fetus a muscular tunic lies about the mesonephric duct cephalad to the ampulla (Fig. 6). This tunic consists of a broad inner longitudinal and a

thin outer circular layer. Along the course of the dilated ampulla the muscular tunic becomes relatively indistinct. In the same fashion a stroma of spindlelike cells is found about the duct above the ampulla (Fig. 6, *A*); there is little or no stroma about the canaliculi which branch off into the lower cervix.

In studying serial sections of fetal uteri stained with a trichrome stain (Milligan) it was noted that the stromal and muscular constituents of the mesonephric duct tend to persist after degeneration of the epithelial elements. As a result of this observation it was possible to follow the degenerating mesonephric duct in the uterine wall for some distance above the ampulla.

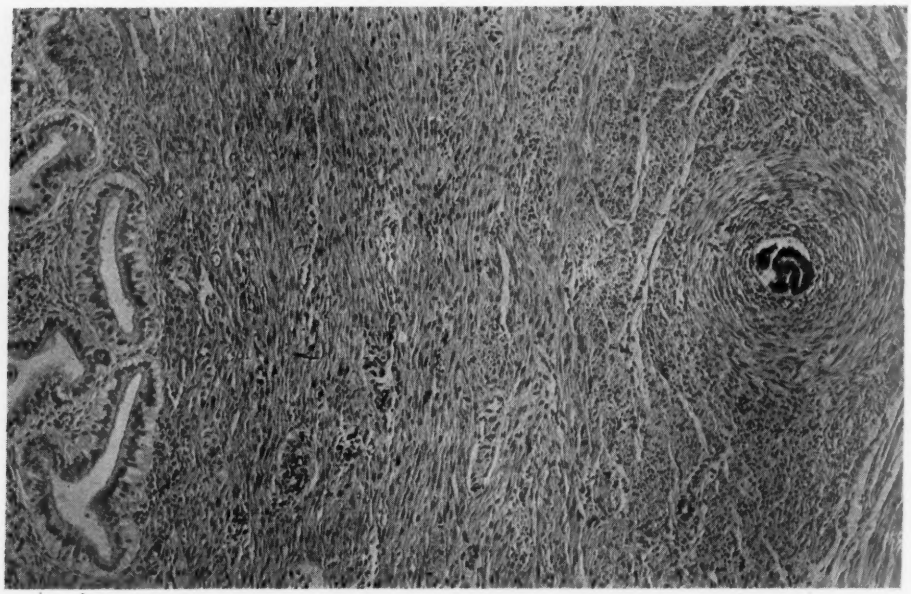


Fig. 4.—In the older embryo (7 months) the middle portion of the mesonephric duct may persist in the uterine wall. In this photomicrograph the mesonephric duct above the ampulla is seen as a curved canal lined by columnar epithelium and surrounded by a stroma of spindle-like cells. It has a distinct muscular tunic. The cervical glands are on the left.

The epithelium lining the duct cephalad to the ampulla consists of a single layer of cylindrical cells with oblong, almost rod-shaped nuclei (Fig. 6, *B*). The cells are highest in the dilated ampullar portion, while in the tubular ramifications the height of the epitheium is less and is proportional to the size of the tubular lumen. In the narrowest twisted tubules the epithelium is low cylindrical or cuboidal. In this cuboidal epithelium the nuclei tend to be spherical or ovoid. In the smallest tubules the cells of the epithelial lining often appear fused.

After reviewing the literature with the published case reports and studying the material available in this laboratory, it appears that remnants of mesonephric origin may be found in the adult cervix either as persistent fetal structures or as new growths arising from fetal residues. Those remnants which are not neoplastic may occur in several different forms. They may be seen as occasional small isolated tubules or canaliculi (Fig. 7, *A*) either in the middle portion of the cervical wall or near the mucosa in the region of the internal os. These isolated tubules are distinguished from the cervical glands (Fig. 7, *B*) by their

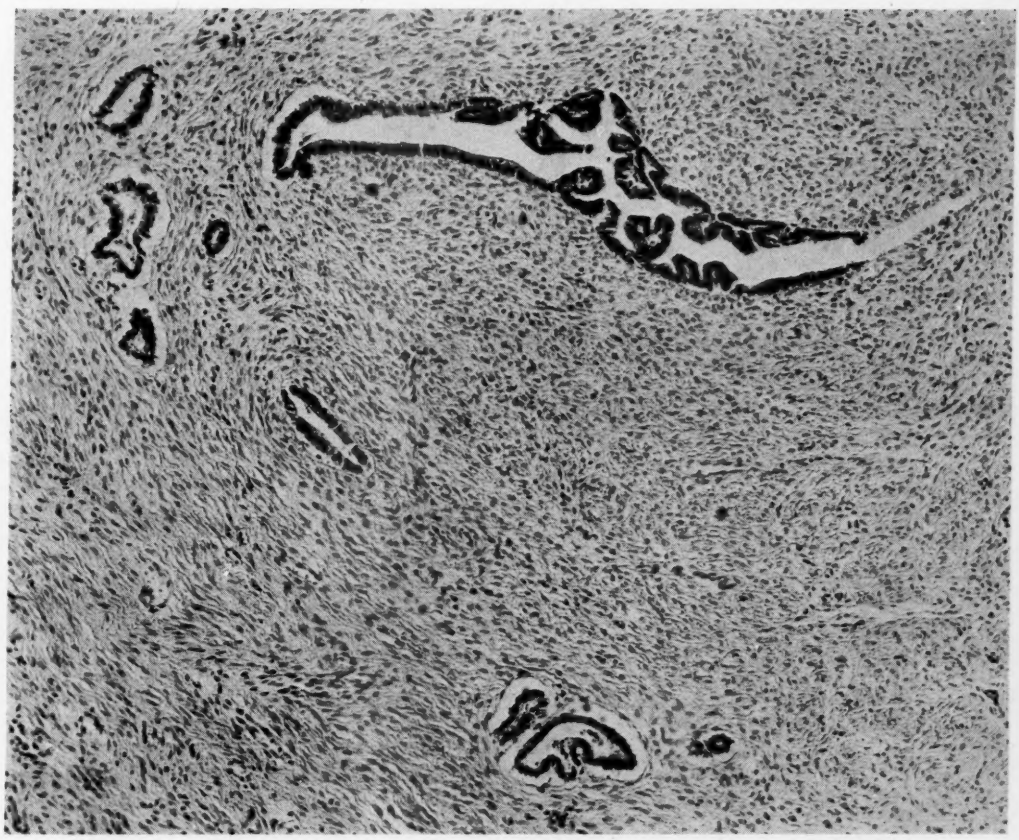
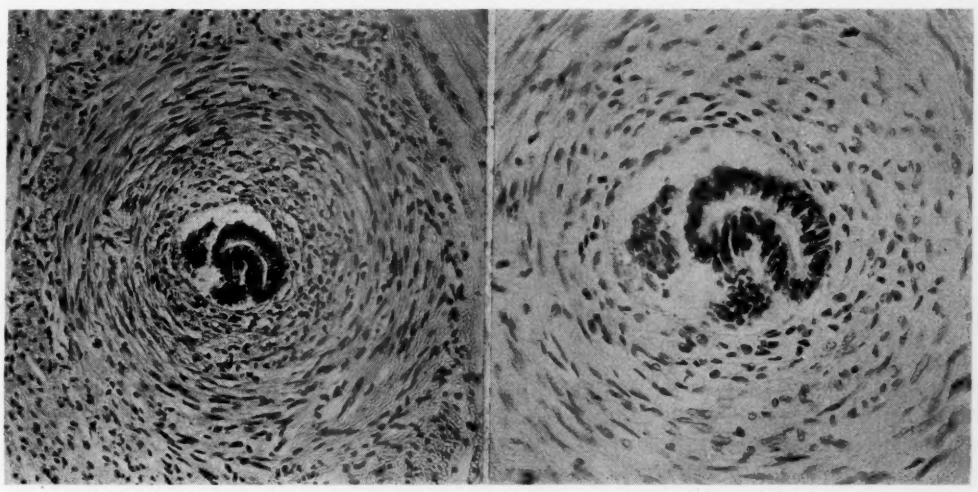


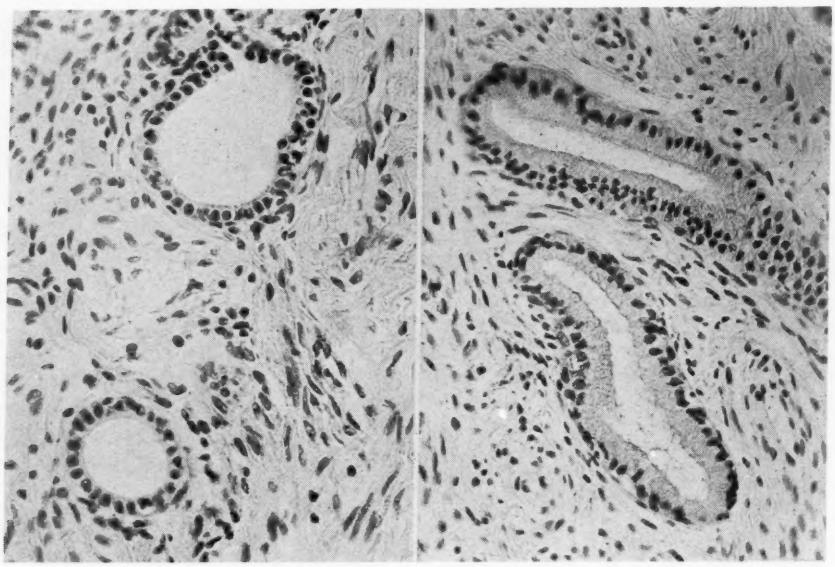
Fig. 5.—When the mesonephric duct persists in the cervix of older embryos it forms a cleftlike ampulla which has, in cross section, slight bends and curves and the beginnings of a few diverticula. Occasional tubules branch off from it. (Photomicrograph of a cross section through the cervix of a 7-month fetus).



A. *B.*

Fig. 6.—In the fetus the mesonephric duct cephalad to the ampulla has a distinct muscular coat, *A*. The epithelium lining the duct lumen is made up of columnar cells with oblong almost rod-shaped nuclei. A stroma of spindlelike cells lies between the epithelium and the muscular tunic, *B*.

distinctive low cuboidal epithelial lining and by their failure to take a mucicarmine stain. Often those scattered tubules lying in close proximity to the glands of the uterine isthmus so resemble the latter as to make differentiation between them difficult. More deeply within the cervical musculature closely approximated cystic dilations of several ampullar tubules with occasional smaller tubules about them may be found (Fig. 8). These have, again, a typical nonsecretory low columnar epithelium. Differentiation between these ampullar tubules and cervical glands is less difficult than is the differentiation between isthmic glands and isolated mesonephric ampullar tubules near the mucosa.



A. *B.*

Fig. 7.—Occasional isolated mesonephric ampullar tubules, *A*, may be found in the cervix. These tubules are distinguished from cervical glands, *B*, by their low cuboidal epithelium which is composed of cells with large distinctly staining nuclei and by their lack of secretory activity. The cells of the mesonephric ampullar tubules do not take a mucicarmine stain, while those of the cervical glands stain vividly with mucicarmine.

The cells which line the tubules lying within the cervical musculature are similar to the cells of the fetal structures described above: there is a single layer of low cuboidal epithelium (Fig. 9) which has a clear translucent cytoplasm with a spherical to egg-shaped dark-staining large nucleus. When stained with iron hemotoxylin the nuclei stand out from the clear cytoplasmic background in a characteristic fashion. Mucicarmine staining shows little or no secretory activity, although occasionally a pinkish mass will be found within a tubular lumen. This is in sharp distinction to the epithelium of cervical glands of comparable size where the tall columnar epithelium contains long rod-shaped nuclei occupying but a small portion of the cell. The richness of secretory activity in the epithelium of the cervical glands is well presented by the vividness with which the cells take a mucicarmine stain.

Elongated narrow clefts with surrounding small tubules (Figs. 10 and 11) lying in the middle muscle layers of the cervix are most characteristic of all of the fetal remnants of the mesonephric ampulla in the adult cervix. These are counterparts of the spurs which the ampulla sent downward into the cervix in

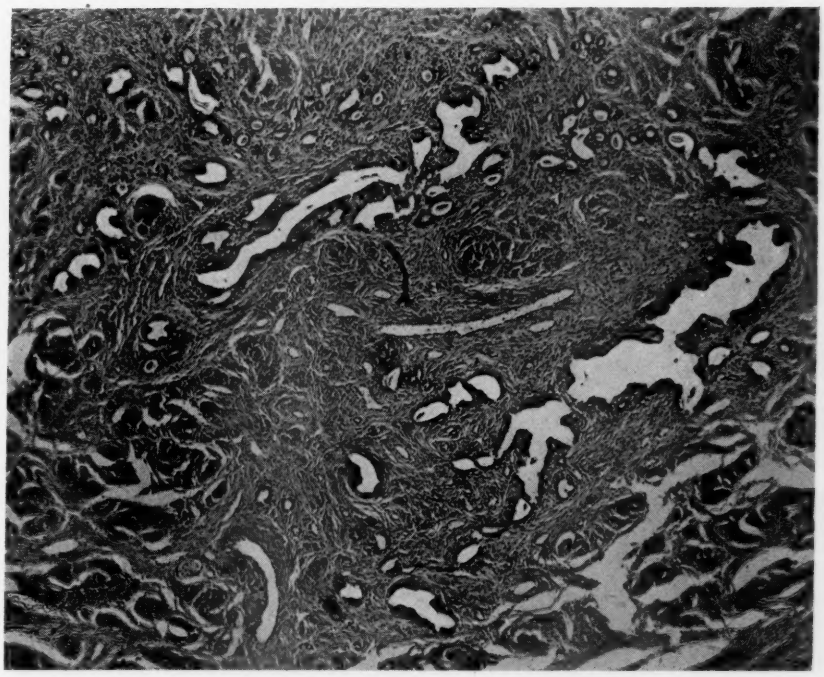


Fig. 8.—Remnants of the mesonephric duct in the adult cervix often occur as cystic dilations of the ampullar tubules with smaller tubules about them. This photomicrograph is from one side of a serially sectioned cervix which contained bilateral mesonephric remnants. (See Fig. 12.)

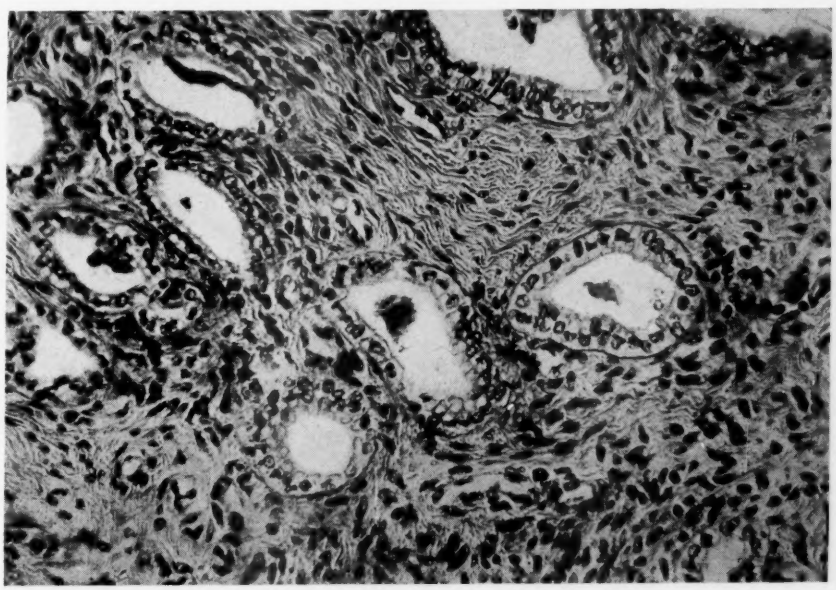


Fig. 9.—The mesonephric ampullar tubules in the cervix are lined by a single layer of low cuboidal epithelium whose cells have clear translucent cytoplasm and spherical or ovoid-shaped large dark-staining nuclei.

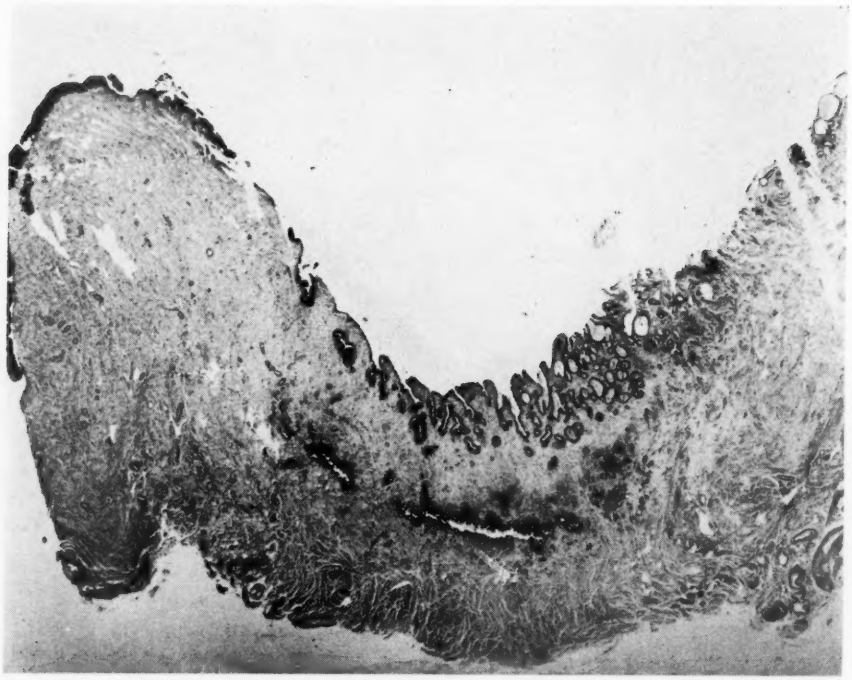


Fig. 10.—A longitudinal section through a cervix to show a mesonephric remnant in the mid-cervical wall. In this instance there is a persistence of a narrow cleftlike large tubule which is surrounded by numerous small canaliculi. (See Fig. 11.)

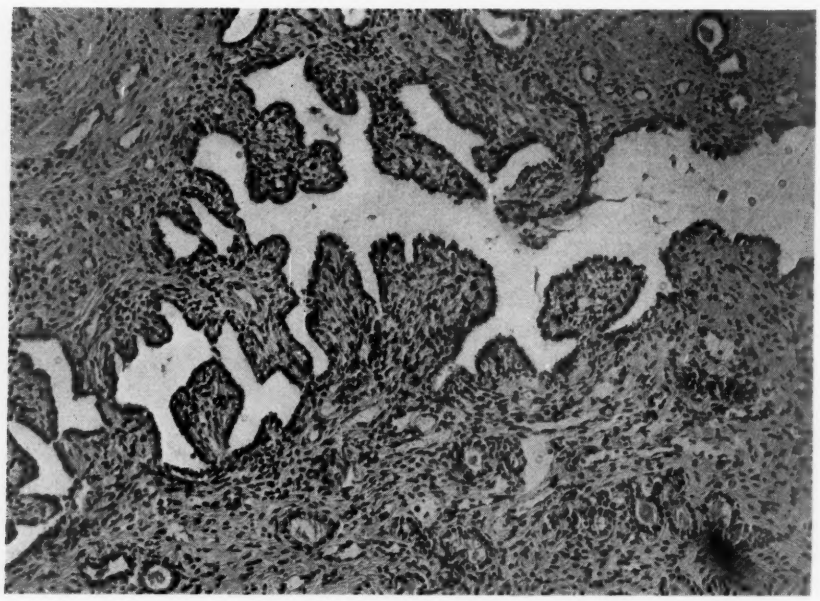


Fig. 11.—The cleftlike mesonephric passages in the adult cervix are remnants of the spurs which the ampulla sent downward into the fetal cervix. They have small canaliculi surrounding them. (See Fig. 10.)

late fetal life. The lining epithelium of these cleftlike structures resembles that of the tubules except that the columnar epithelium is often higher and the nuclei of the cells making up the epithelium tend to be more rod shaped.

Usually the persistent mesonephric remnants are found in only one wall of the cervix. However, in one serially sectioned cervix included in this report, bilateral cervical remnants were discovered (Fig. 12). In this specimen it was possible to follow the mesonephric duct structures from the vicinity of the internal os to the lower portion of the portio vaginalis. The tubules lay in the musculature of the middle portion of each lateral cervical wall. They corresponded in position and in structure to the fetal mesonephric ducts observed in serially sectioned embryonic uteri.

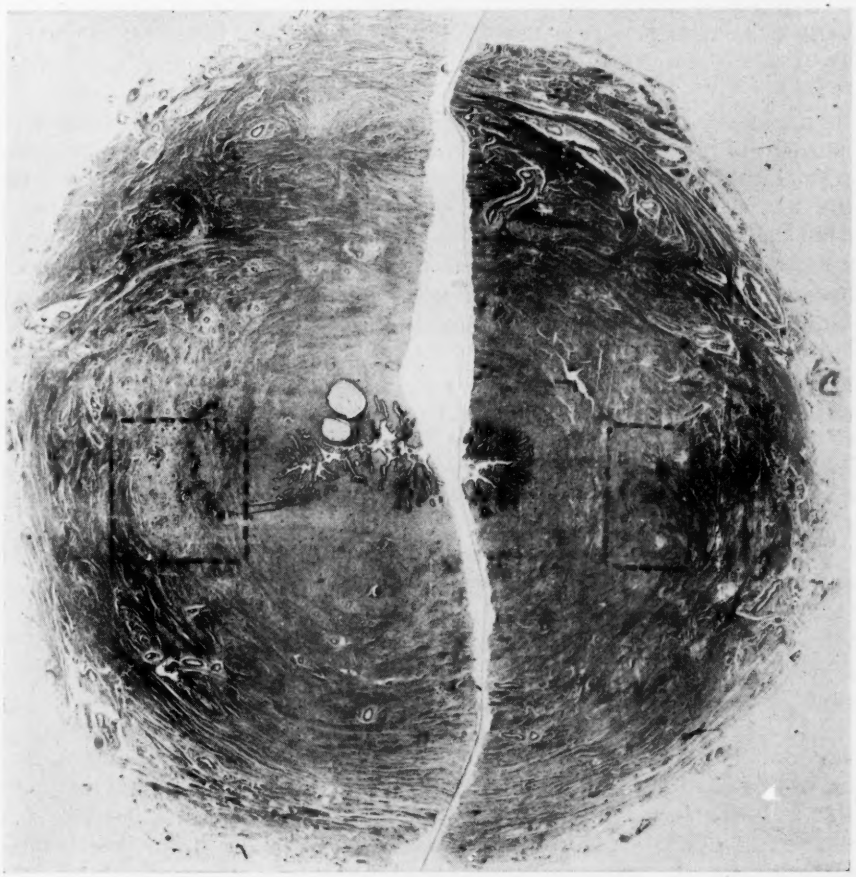


Fig. 12.—Cross section through the two halves of a serially sectioned adult cervix. The boxed areas contain bilateral persistent mesonephric duct tissue which has the same histologic structure as found in the fetus. (See Fig. 8.)

There is considerable variation in the reported incidence of persistent mesonephric ducts in the cervix. In a series of fifty-four adult uteri examined specifically for mesonephric remnants, Meyer found portions of the duct in twelve specimens. Rieder[7] noted similar rests in 20 per cent of the specimens he studied. Maudach[8] reported mesonephric rests in 40 per cent of the uteri from all newborn and older children he examined. Fischer,[9] on the other hand, found a mesonephric duct in but one adult uterus of fifty which he inspected.

There were five nonneoplastic mesonephric duct remnants in the 1,192 specimens examined in this laboratory. In a series of 1,413 cervices examined by Wolfe, "only one contained normal remnants of Gärtner's duct." It would appear that the earlier workers held a unanimity of opinion as to the presence of mesonephric residues in the adult cervix but that they disagreed notably as to the frequency of such remains. They were in agreement in stating that these residues were for the most part comparable in structure with the mesonephric tissues found in the fetus near term. That neither Wolfe nor I found mesonephric tissues in the cervix with a frequency comparable with that of Meyer and others may be due to the fact that our specimens were from surgical pathologic material and that we had access to but one or two blocks cut from each cervix. It is quite probable that our incidence would more closely approximate Meyer's if we had serial sections from each of the cervices in our series. In addition in the series reported here, all specimens difficult to differentiate (particularly where there were questionable tubules near the isthmic glands) were discarded.

It is necessary to differentiate between a simple remnant of a fetal structure in the adult and a neoplasm arising from such a tissue. Meyer[10] makes this distinction particularly evident in discussing the persistence of mesonephric cervical remnants when he points out the difference between the factors leading to the prevention of the normal disappearance of fetal tissue (phylogenetic autonomy) and those factors leading to tumor formation (pathologic cellular autonomy).

Three types of neoplasms of mesonephric duct origin may be expected to develop in the uterus—cysts, adenomatous proliferations of varying degree, and adenocarcinomas.

A cystadenoma developing from rests of wolffian duct origin in the cervix is reported by Dworzak.[11] Henkel[12] described a "hypertrophia portionis cystica" which he stated was a cystic transformation of cervical rests arising from the wolffian duct. Stubler,[13] Kuster,[14] Arx,[15] Combert,[16] Knauer,[17] Gudim-Lewkowitsch,[18] Klein,[19] von Recklinghausen,[20] and others have also reported cysts of the uterus which presumably were of mesonephric duct origin. Critical review of most of these case reports, however, makes it difficult to determine whether or not the neoplasms actually originated in the cervix or whether they developed in the lateral uterine wall.

Criteria have been established for the diagnosis of uterine cysts of mesonephric origin by Meyer, Dworzak, and Klein. They state that for such cysts to be topographically correct they should lie in the longitudinal axis of the uterus, they should have a serpentine or corkscrew course, and they should be lined by columnar epithelium characteristic of the lining of mesonephric structures; there may, in addition, be a scattering of surrounding muscle and stroma which resembles that surrounding the fetal mesonephric duct above the ampulla. One specimen in the 1,192 examined in this laboratory showed cystic cavitations in the lateral uterine wall beginning below the level of the internal os and extending upward in the myometrium to a point approximately midway between the internal os and the fundus (Fig. 13). The serpentine course of the cystic cavitations in the uterine wall and the low cuboidal epithelium lining the cystic cavities suggested that this was a cystic mesonephric duct remnant.

Meyer mentions that occasional isolated mesonephric ampullar tubules tend to be cystic. He states that while these cystic changes are occasionally found in the fetus, they are much more common in the adult. Rarely are the cysts larger than 2.5 mm. in diameter. Differentiation between these cysts and deeply placed isolated cysts of the cervical glands is not always easy. Mixed cysts may occur in which there is a fusion of mesonephric duct cysts with glands of the cervix.

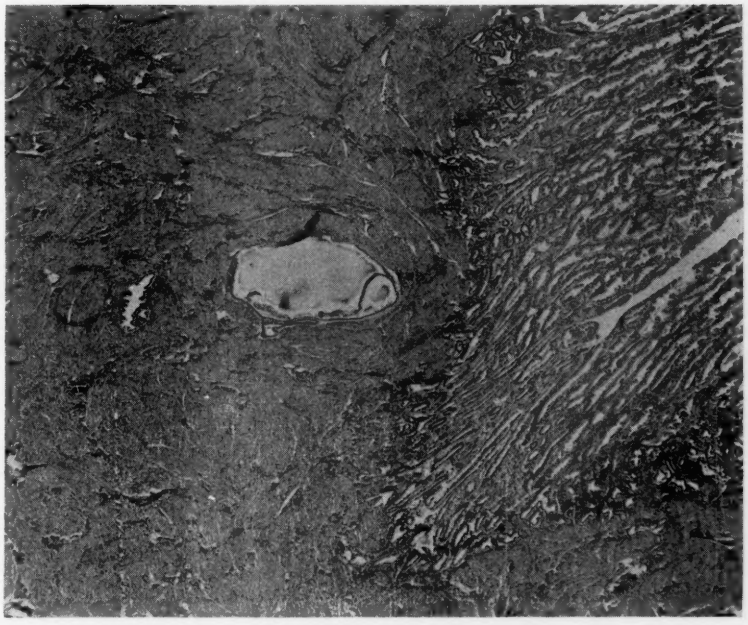


Fig. 13.—Photomicrograph through the uterine wall showing a cystic cavitation which, beginning below the level of the internal os, extended for a distance of 2 cm. cephalad. The irregular course of the cavitation and the low cuboidal epithelium which lined it suggested that this was a cystic mesonephric duct remnant.

Fig. 14.—Adenomatous hyperplasia of mesonephric duct remnants in the cervix develops as masses of small tubules infiltrating the cervical wall. In this section through the mid-portion of the postero-lateral cervical wall minute tubules lie in groups throughout the musculature. (See Fig. 15).

Adenomatous hyperplasia of mesonephric duct remnants in the cervix occurs as a conglomerate mass of closely packed small tubules or canaliculi which may be found either near the cervical mucosa or, more often, in the middle layers of the cervical musculature (Fig. 14). These adenomatous proliferations rarely become tumors of appreciable size and are most often discovered in the course of histologic examination of cervical tissues removed either for biopsy or at the time of amputation of an unhealthy cervix. The tubules or canaliculi usually lie in groups in the interstices of the cervical musculature. There may be, however, occasional isolated masses of closely packed tubules near the endocervical mucosa. Microscopically the tubules are small and are round or ovoid in shape. While they may vary in diameter from capillary size to macroscopic cysts, a distinguishing characteristic which I have seen has been the tendency for most of the tubules to be approximately the same diameter. When larger tubules are present they may show outpouchings and diverticula. There is little or no musculature about the tubules and scanty or no stroma. When stroma is present, as described by Rust,[27] it is of a spindle or round cell character similar to that seen about the duct above the ampulla. Rarely a long narrow ductlike cleft will be discovered in the midst of an adenomatous proliferation; such a ductlike remnant may be the remains of the ampullar cleft seen in the fetus.

The tubules (Fig. 15) which comprise these adenomatous hyperplastic formations are lined by a single layer of cylindrical epithelium. The cells are low cuboidal in type and the individual cells contain a translucent pale cytoplasm with a large round or coffee bean-shaped nucleus which fills much of the cell body.

The nuclei are rich in chromatin and stain intensively. An occasional tubule will show some secretory activity as evidenced by a mucicarmine staining of its contained secretion; for the most part, however, the tubular lumina are empty and the cells do not take a mucicarmine stain.

Meyer, Klein, and Thumin described cervical adenomas of mesonephric origin many years ago. More recently, Rust, Rockstroh, Reeb, and Wolfe have reported similar ones. In each of these reports the findings are essentially as described here both as to origin and structure of the neoplasm. In none was the diagnosis made prior to histopathologic examination of the excised tissues.

There were four cervices which contained adenomatous hyperplasias of mesonephric duct origin among the 1,192 specimens examined in this laboratory. In one of these the major portion of the posterolateral cervical wall was infiltrated by innumerable minute twisted tubules having the typical histologic picture just described; the other three contained areas in which there were compact masses of canaliculi having a topographic location and microscopic appearance compatible with a diagnosis of adenomatous hyperplasia of mesonephric ampullar tubules.

Adenocarcinomas may develop from mesonephric duct remnants in the cervix. Grossly the tumor has usually been found (in those cases reported where the neoplasm had not as yet involved the entire cervix) in the anterolateral or posterolateral midcervical walls. The growth is a gray-white or brownish friable area which can be differentiated from the remainder of the cervix. Microscopically the tumor consists almost entirely of masses of glandlike tubules which are packed closely together. These tubules show an unorganized arrangement and are of varying sizes, many having distended lumina while the lumina of others are narrowed or obliterated by the many layers of cells forming the tubular wall. In some areas epithelial proliferations or papillary extrusions project into the tubular lumina. The cells and tubules lie in the fibromuscular connective tissues of the cervix and tend to invade between the muscle bundles.

The epithelium lining the tubules is bi- and multi-striated throughout and is marked by unusual irregularity in the height of the cells and the position of the nuclei. The cell nuclei are for the most part large lightly staining and contain an increased number of mitoses. Mucicarmine staining shows no evidence of any appreciable amount of mucus in the cells, but in many places the lumina have a thin mucuslike layer on the epithelial surface; this layer takes a light pinkish stain with mucicarmine.

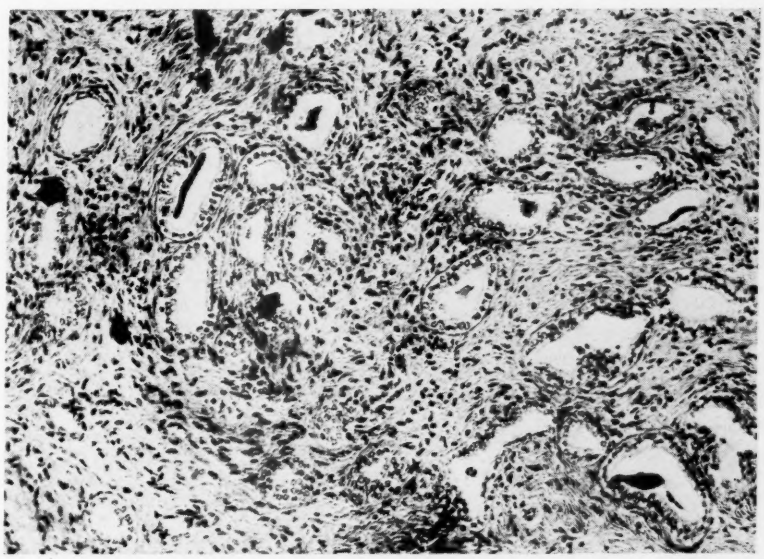


Fig. 15.—The tubules making up an adenomatous hyperplasia of mesonephric duct remnants in the cervix are often found in closely packed masses. They are lined by a single layer of low cylindrical or cuboidal nonsecretory epithelium, the cells of which have a pale cytoplasm and large round or ovoid well-staining nuclei. (See Fig. 14).

The first report of a carcinoma of the ampulla of the mesonephric duct was made by Meyer in 1903.[21] The same author reported a second case in 1907.[22] In the first instance the nature of the tumor was recognized by the fact that the upper part of the mesonephric canal was still intact and that the adenomatous glandular proliferation arising from it gradually merged into a destructive neoplasm of the cervix and portio which had the characteristics of the tumors described. The second case was histologically similar to the first. Danneel[23] also describes an adenocarcinoma of the cervix which was assumed to have developed from mesonephric duct remnants because of its position and structure. This opinion was concurred in by Meyer who saw sections of the neoplasm. Wagner, in 1929[24] and Rockstroh, in 1935[25] reported similar tumors.

One adenocarcinoma of the cervix having an architectural pattern suggesting origin from a mesonephric remnant was among the 1,192 specimens examined for this presentation. The tumor, discovered in routine sections, invaded but a small portion of the posterolateral wall of the cervix at the level of the internal os. It consisted of strands and masses of glandlike tubules (Fig. 16) extending into the substance of the cervix and invading the lower corpus. The lining of the tubules is composed of cuboidal and low columnar cells of irregular height having large pale-staining nuclei. There are numerous mitoses. In many places the configuration of the tubular structure is lost. The neoplasm invades between

the muscle fibers of the cervix. The assumption that this carcinoma developed from rests of mesonephric duct origin (insofar as such a diagnosis can be made in the absence of typical normal mesonephric tissue) is based on the position of the tumor and its architectural pattern. It shows no similarity to the usual malignancies arising from mucous glands. It has striking similarity in appearance to the case described by Meyer in which an adenocarcinoma could be identified as arising from a still intact mesonephric remnant.

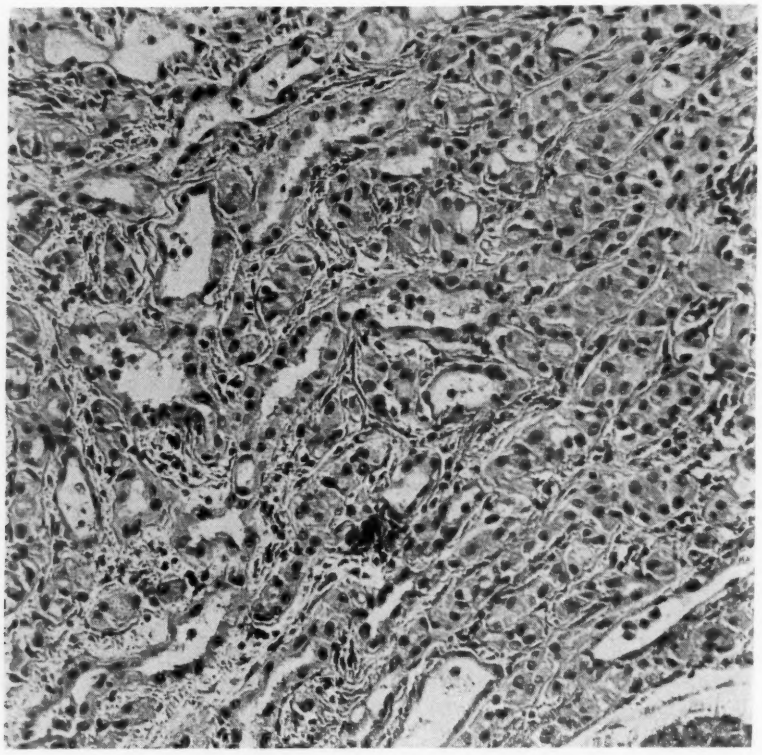


Fig. 16.—Adenocarcinoma of mesonephric duct origin in the cervix consists of masses of glandlike tubules which are closely packed. These tubules have a disorganized arrangement, are of varying sizes, and their lumina may be obliterated by many layers of cells.

Discussion

A fetal remnant which is homologous with a portion of the male genitals and which, instead of degenerating in a normal fashion, persists in the adult female should logically be diminutive in size and embryonic in character. The exact homology of the mesonephric ampulla in the female has not been demonstrated. The hypothesis has been advanced that it is homologous with either the ampulla of the vas deferens or the seminal vesicle. If this contention is accepted it would be assumed that tissues resembling the fetal mesonephric structures would be found. Furthermore it would not be anticipated that the development of the embryonic structures would progress beyond a late stage in female embryonic development. Rather, inasmuch as the remnants disappear

in most individuals, those which do occasionally remain, unless undergoing neoplastic changes, would tend to be small in size and poorly developed.

It is not within the scope of this presentation to attempt to explain why fetal remnants of the mesonephros persist in some women and not in others. Meyer has attempted an explanation of the phenomenon on the basis of the prevention of the normal disappearance of fetal parts by a particular stimulus located either in the vicinity of the fetal structure or else within the cells of the structure itself; this hypothesis is gone into in considerable length in his monograph entitled *Ueber epitheliale Gebilde im Myometrium einschliesslich des Gärtnerschen Ganges* published in 1899. That remnants of the mesonephric duct do persist in the fetal cervix has been well demonstrated by Meyer, Maudach, and Rieder. Study of serially sectioned fetal uteri reaffirm their observations. The definitive evidence in support of their efforts would be wax model reconstructions prepared from serial sections of the fetal and adult cervices containing mesonephric remnants; such a project is at present under way in this laboratory.

A number of case reports have appeared during the past half century giving histologic descriptions of tumors similar to those first described by Meyer. There are now a sufficient number of these to warrant the acceptance of mesonephric duct remnants in the cervix as a histopathologic entity. In order to facilitate further investigation a table of published case reports is included herewith (Table I).

TABLE I. PUBLISHED CASE REPORTS OF MESONEPHRIC DUCT REMNANTS IN THE ADULT HUMAN CERVIX

AUTHOR	REFERENCE
Persistent Fetal Elements (Not Neoplastic)	
Rieder, C.	Virchows Arch. **96:** 100, 1884.
Maudach, F. V.	Virchows Arch. **156:** 94, 1899.
Meyer, R.	Ztschr. f. Geburtsh. u. Gynäk. **42:** 526, 1900.
	Ztschr. f. Geburtsh. u. Gynäk. **58:** 527, 1906.
	Arch. f. mikr. Anat. u. Entwges. **73:** 751, 1909.
Wolfe, S. A.	Am. J. Obst. & Gynec. **39:** 312, 1940.
Cysts of Mesonephric Duct Origin (Doubtful Omitted)	
Dworzak, H.	Arch. f. Gynäk. **157:** 162, 1934.
Henkel, M.	Arch. f. Gynäk. **113:** 427, 1920.
Adenomas	
Meyer, R.	Ztschr. f. Geburtsh. u. Gynäk. **37:** 332, 1897.
	Ztschr. f. Geburtsh. u. Gynäk. **42:** 526, 1900.
Klein, G.	Virchows Arch. **154:** 189, 1898.
Thumin, L.	Arch. f. Gynäk. **61:** 15, 1900.
Rust, W.	Arch. f. Gynäk. **162:** 350, 1936.
Rockstroh, H.	Ztschr. f. Geburtsh. u. Gynäk. **112:** 95, 1935.
Reeb, M.	Gynéc. et obst. **36:** 401, 1937.
Wolfe, S. A.	Am. J. Obst. & Gynec. **39:** 312, 1940.
Adenocarcinomas	
Meyer, R.	Virchows Arch. **174:** 270, 1903.
	Ztschr. f. Geburtsh. u. Gynäk. **59:** 234, 1907.
Wagner, G.	Zentralbl. f. Gynäk. **53:** 1336, 1929.
Froboese, H.	Gesellsch. f. Gynäk., Berlin **12:** 4, 1934.
Danneel, H.	Arch. f. Gynäk. **159:** 395, 1935.
Rockstroh, H.	Ztschr. f. Geburtsh. u. Gynäk. **112:** 95, 1935.

In the classification of mesonephric remnants in the cervix differentiation should be made between nondegenerated fetal structures (occasional tubules, portions of persistent ducts, and scattered canaliculi) and new growths arising from such structures (cysts, adenomatous proliferations, and adenocarcinomas).

In 1,192 cervices there were five specimens in which mesonephric remnants were found, one cyst of the cervicocorporeal uterine wall presumably of mesonephric origin, four adenomatous proliferations of mesonephric ampullar tubules, and one adenocarcinoma of the cervix which architecturally and topographically was of mesonephric origin. Detailed case reports have not been included because they are similar in all respects to the general description of each entity included in the text.

The diagnosis of a remnant of mesonephric tissue or a tumor arising from such a remnant will rarely be made grossly. The diagnosis is obviously a histopathologic one. It will be made for the most part during the course of histologic study of "routine" sections. If but one block of tissue is taken through the lower posterior lip of the cervix, as is customarily done in examining cervices which are not suspected of harboring a malignancy, these interesting lesions will frequently be missed. It is quite probable that Meyer's statement that 20 per cent of all cervices have mesonephric remnants in them is more nearly correct than the incidence of approximately 1 per cent that I am reporting.

The identification of typical mesonephric duct remnants in the cervix is not difficult. The location of the tubules in the midportion of the lateral cervical wall is characteristic. Characteristic also are the small rounded canaliculi lined by nonsecretory occasionally ciliated low columnar or cuboidal cells with their translucent cytoplasm and large, round, clearly staining nuclei.

Summary and Conclusions

This presentation is an attempt to portray the embryology, the histology, and the microscopic pathology of mesonephric remnants in the uterine cervix. In order to accomplish this the literature has been reviewed, serially sectioned tissues have been studied, and sections from 1,192 surgically excised cervices have been examined.

The presence of an ampulla of the mesonephric duct in the fetal cervix has been demonstrated by Meyer and others. Study of serially sectioned fetal uteri confirms their observations. Remnants of these fetal elements may persist in the adult cervix either as nondegenerated structures or as neoplasms arising from such residues. These remnants will ordinarily be discovered during study of routine sections of the cervix. The characteristic histologic appearance of mesonephric remnants in the cervix is that of small tubules or canaliculi lined by a typical low columnar nonsecretory epithelium consisting of cuboidal cells containing a translucent pale cytoplasm and large well-staining ovoid or round nuclei. These tubules can be differentiated from cervical glands. The histopathologic appearance of neoplasms arising from these remnants is given in detail.

Five cases of mesonephric remnants in the cervix and five neoplasms arising from mesonephric remnants in the cervix are added to the literature.

There is now sufficient evidence to warrant acceptance of mesonephric duct remnants in the cervix as a histopathologic entity.

References

1. Meyer, R.: Ztschr. f. Geburtsh. u. Gynäk. **42**: 526, 1900.
2. Meyer, R.: Die pathologische Anat. d. Gebarmutter, Handbuch der spez. path. Anat. u. Histol., vol. 7, part 1, Henke u. Lubarsch. Berlin, J. Springer, 1924, p. 43.
3. Meyer, R.: Handb. d. Gynäk., vol. 6, part 1, W. Stoeckel, München, J. F. Bergman, 1926, p. 651.
4. Wolfe, S. A.: Am. J. Obst. & Gynec. **39**: 312, 1940.
5. Meyer, R.: Arch. f. mikr. Anat. u. Entwges. **73**: 751, 1909.
6. Meyer, R.: Ztschr. f. Geburtsh. u. Gynäk. **58**: 527, 1906.
7. Rieder, C.: Virchows Arch. **96**: 100, 1884.
8. Maudach, F. v.: Virchows Arch. **156**: 94, 1899.
9. Fischer (quoted by Meyer): Ztschr. f. Geburtsh. u. Gynäk. **37**: 327, 1897.
10. Meyer, R.: Ueber epitheliale Gebilde im Myometrium des fötalen und kindlichen Uterus einschliesslich des Gartnerschen Ganges, Berlin, 1899, S. Karger.
11. Dworzak, H.: Arch. f. Gynäk. **157**: 162, 1934.
12. Henkel, M.: Arch. f. Gynäk. **113**: 427, 1920.
13. Stubler, H.: Zentralbl. f. Gynäk. **47**: 1068, 1923.
14. Kuster, F.: Ztschr. f. Geburtsh. u. Gynäk. **80**: 666, 1918.
15. Arx, W. v.: Ztschr. f. Geburtsh. u. Gynäk. **79**: 52, 1917.
16. Combert, S.: Inaug. Diss., Abs. Zentralbl. f. Gynäk. **44**: 1271, 1920.
17. Knauer, E.: Zentralbl. f. Gynäk. **19**: 498, 1895.
18. Gudim-Lewkowitsch, D.: Abs. Zentralbl. f. Gynäk. **38**: 1048, 1914.
19. Klein, G.: Virchows Arch. **154**: 189, 1898.
20. v. Recklinghausen (quoted by Dworzak): Die Adenomyome und Cystadenome der Uterus und Tubenwandung, ihre Abkunft von Resten des Wolffschen Körpers, Hirschwald, Berlin, 1896.
21. Meyer, R.: Virchows Arch. **174**: 270, 1903.
22. Meyer, R.: Ztschr. f. Geburtsh. u. Gynäk. **59**: 234, 1907.
23. Danneel, H.: Arch. f. Gynäk. **159**: 395, 1935.
24. Wagner, G.: Zentralbl. f. Gynäk. **53**: 1336, 1929.
25. Rockstroh, H.: Ztschr. f. Geburtsh. u. Gynäk. **112**: 95, 1935.
26. Reeb, M.: Gynéc. et obst. **36**: 401, 1937.
27. Rust, W.: Arch. f. Gynäk. **162**: 350, 1936.
28. Thunin, L.: Arch. f. Gynäk. **61**: 15, 1900.
29. Froboese, H.: Gesell. f. Gynäk., Berlin **12**: 4, 1934.

Discussion

HAROLD L. GAINEY, M.D., Kansas City, Mo.—Mesonephric duct remnants in the adult female are a phylogenetic anomaly. The cranial end is normally encountered in the mesovarium and the lateral third of the mesosalpinx forming the epoöphoron. Caudad in the vagina, it again appears in the more familiar form of Gartner's duct cysts. That wolffian duct remnants persist in the cervix "is less commonly recognized" as stated by the author and readily accepted by our own experience and with Wolfe's report of one in 1,413 cases. Wolfe's explanation for his low incidence and my inability in several large pathology departments to find one case is that in routine sections of the cervix the area likely to be affected is not studied.

Dr. Huffman in this excellent presentation has made a definite contribution to American gynecologic literature. His review of the literature and presentation of the results of studies resulting from serially sectioning 1,192 surgically excised cervices are given. Five cases of mesonephric remnants in the cervix and five neoplasms (one malignant) arising from mesonephric remnants in cervix are added to the literature.

This paper should arouse interest in more extensive studies of the uterine cervix, and with the increase in complete hysterectomy, opportunities for such studies will be more frequent.

The morphologic and the cytologic characteristics have been clearly demonstrated and described. Outlined are such details as the presence of a muscular tunic with a stroma of

spindlelike cells above the ampulla and their absence or presence in small amounts below the ampulla. The character of the epithelial elements varying from a single layer of cylindrical cells with oblong rod-shaped nuclei to low cuboidal with ovoid nuclei, with failure to take mucicarmine stain, while the glandular structures of the cervix do, aids in identification and differentiation of these structures.

The anatomic and pathologic significance of this presentation can be readily accepted. The clinical significance may be even greater than would be suggested by the low incidence of occurrence, 1 per cent. Further studies of malignant tumors of the cervix, particularly adenocarcinoma, might possibly reveal a higher percentage having origin from this source. A recently studied, yet to be reported, mesodermal mixed tumor of the uterus, when reviewed in the light of this paper, contained some highly suggestive tubular structures.

I would like to ask Dr. Huffman his reaction to this thought.

DR. HUFFMAN (Closing).—I wish to thank Dr. Gainey for his discussion and wish I might have summarized the material I presented as adequately as he has done. Dr. Gainey's description of a mixed tumor of the uterus containing tubular elements strongly suggests that it originated from a persistent mesonephric duct remnant. Undoubtedly mesonephric remnants in the uterus are frequently missed in the study of "routine" sections. The rarity with which multiple sections are taken from supposedly normal tissues surely must result in many similar omissions of other equally interesting pathologic entities.

ABDOMINAL COLPOCYSTOPEXY FOR COMPLETE PROLAPSE OF THE VAGINA AND BLADDER*

The Rectus Suspension Principle of Crossed-Suspender Support

PAUL F. FLETCHER, M.D., M.G.O., F.A.C.S., ST. LOUIS, MO.

(From the Department of Obstetrics and Gynecology, St. Louis University School of Medicine, and the St. Louis County Hospital)

COMPLETE prolapse of the vagina is characterized by eversion of its walls to such an extent as to cause complete exteriorization and eversion. The condition occurs most frequently in women who have undergone hysterectomy. It also occurs in women whose genital organs have not been subjected to surgical mutilation, but we are considering only those cases in which hysterectomy has been performed. The important factor involved pertains to the complete eversion of the anterior vaginal wall and bladder (Fig. 1). It is the correction of this condition with which we are primarily concerned.

Prolapse of the posterior vaginal wall may be mistaken for rectocele even though the protrusion originates above the level of the rectum (Figs. 1, 3*A*, and 4). Rectocele is due to relaxation of the pubococcygeal portion of the levator diaphragm combined with defects in the perineal body and rectovaginal septum. When these are intact and the unsupported vaginal wall bulges into the vagina, a hernia (enterocele) is present (Figs. 2 and 4).

Anatomical Considerations

The following points should be considered.

1. Eversion of the anterior wall of the vagina carries the bladder with it. When prolapse is complete, the bladder is situated almost entirely outside the pelvic cavity (Figs. 1 and 3*A*). Distention of the bladder in this position causes an accentuation of the vaginal protrusion. A sound introduced into the bladder and directed toward the fundus may pass in a direction exactly opposite the normal.

2. Functional difficulties resulting from this abnormal position of the bladder vary from complete or partial retention to fluctuating degrees of incontinence. In almost every case the bladder must be pushed back up into the pelvis before micturition can be satisfactorily accomplished (Fig. 3*A*). Retention predisposes to infection, cystitis, and the formation of vesicle calculi.

3. Eversion of the posterior wall of the vagina may be accompanied by descent of the anterior wall of the rectum, particularly when associated with partial or complete destruction of the perineal body and rectovaginal septum. If these structures are intact, the rectum usually remains in normal position and is not involved. Then the protrusion is caused by a posterior herniation or

*Read before the Central Association of Obstetricians and Gynecologists, Oct. 23, 1947, Louisville, Ky.

Fig. 1.—Complete prolapse of vagina and bladder following total hysterectomy. Scar tissue in upper end of vaginal vault is grasped with tenaculum. Tip of catheter situated just above level of forceps.

Fig. 2.—First patient six years after operation. Small anterior colpocele does not include bladder. Posterior vaginal wall hernia (enterocele) originates above level of rectum. Perineal body is intact. No rectocele present.

Fig. 3*A*.—Schematic illustration to show extent of potential visceral distortion when prolapse of vagina is complete. Kinking of urethra interferes with bladder function. Perineal body and rectovaginal septum are intact. Rectum is not involved in posterior vaginal wall hernia (enterocele).

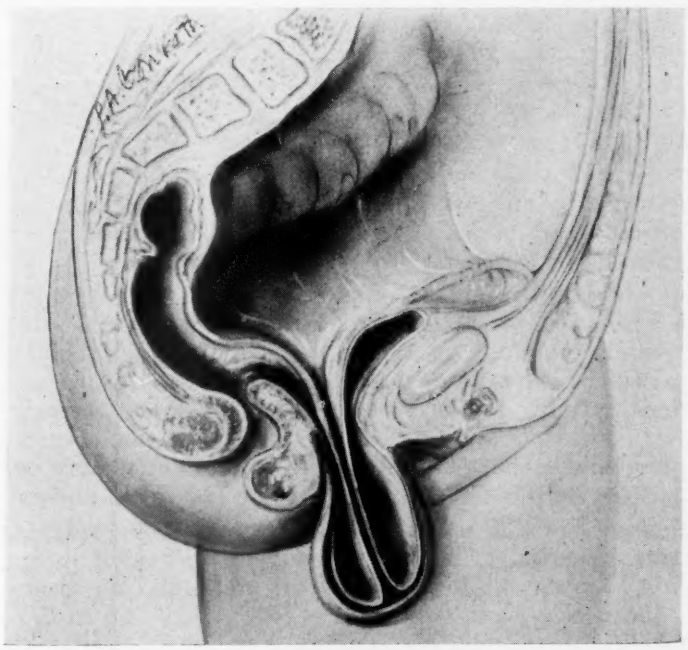


Fig. 3*B*.—Schematic illustration to show intimate connection between anterior vaginal wall and bladder as compared with that which exists between posterior vaginal wall and adjacent pelvic viscera.

enterocele (Figs. 3*A* and 4). It is important to differentiate between rectocele and enterocele because correction of these defects involves two entirely different operative procedures. High colpoperineorrhaphy is required for the former, while complete obliteration of the cul-de-sac, from above, may be necessary in the latter (Figs. 7 and 8). Both procedures may have to be employed if the two conditions coexist.

4. The rectum and vagina are less intimately connected than the bladder is to the anterior vaginal wall because the cellular tissue of the rectovaginal septum is flexible and lax, in order to adapt itself to the rectal movements involved in the act of defecation.

According to Demarest[1] the rectal supports are stronger than those of the bladder because the puborectal fibers of the levator ani are intimately connected with the rectum. Hence displacement of the posterior wall of the vagina and rectum has less significance, clinically, than the downward movement of the bladder with the anterior vaginal wall (Figs. 3*A* and 3*B*).

When looking at the condition from above after the abdomen is opened, the vagina is inverted and the walls descend toward the cervical stump or toward the vaginal cicatrix which is present if the patient has had a complete hysterectomy. A funnel-shaped arrangement is thus encountered with the cervical stump or vaginal cicatrix being in the most dependent position, comparable to the small end of a funnel (Fig. 1). The peritoneum descends into the vaginal funnel covering the bladder; then, after leaving the bladder, it extends on to the posterior wall of the vagina and is reflected upward on to the anterior wall of the rectum and sigmoid. Because the uterus has been removed, the cul-de-sac of Douglas may be elongated. This predisposes to the development of an enterocele. It may or may not be associated with rectocele, since the latter is dependent to a very great extent upon the functional efficiency and anatomical integrity of the perineal body and rectovaginal septum (Fig. 4).

Complete obliteration of the cul-de-sac should be done in these patients if the best ultimate result is to be obtained (Figs. 7 and 8).

Commentary

Berkely and Bonney[12] said, "The possibility of curing a case of prolapse in which the entire uterus has been removed, without narrowing the vagina to a degree which prevents sex relations, is practically nonexistent."

Palsey[2] reported a successful cure of prolapse of the urethra and bladder in a 15-year-old girl by anchoring the anterior wall of the bladder to the periosteum of the pubic bone, as described by Hepburn.[3] In this case the defect was primarily urethral.

Phaneuf[4] stated, "Subtotal colpectomy (LeFort operation) is useful in older women with total prolapse or inversion of the vagina following hysterectomy. The one disadvantage, namely, closure of the vagina, makes it applicable only to those women whose age make sexual relations unimportant." He reported a series of twenty-six cases of subtotal colpectomy and six cases of total colpectomy but he did not say at what age sexual relations become unimportant to women. We believe that colpectomy is unnecessary at any age if the condition of the patient will permit her to be subjected to an abdominal operation.

In the analysis of 730 operations for uterovaginal prolapse which he has performed over a period of twenty-seven years, Phaneuf says, "The rate or recurrence in all operations for prolapse will no doubt increase with the length of time that the patients are observed." He reports two cases of slight recurrence after using Moscheowitz' technique for the correction of a large posterior

vaginal wall hernia. "In neither case was further correction necessary." He goes on to say that "adequate repair of the pelvic floor is essential in all cases unless the perineum is intact and gives good support," and, "Subtotal or total colpectomy are the only operations from which satisfactory results may be expected."

We would like to submit the "rectus suspension principle of crossed-suspender support" as a dependable surgical procedure in the treatment of complete prolapse of the vagina and bladder following hysterectomy for patients in whom an abdominal operation is not contraindicated.

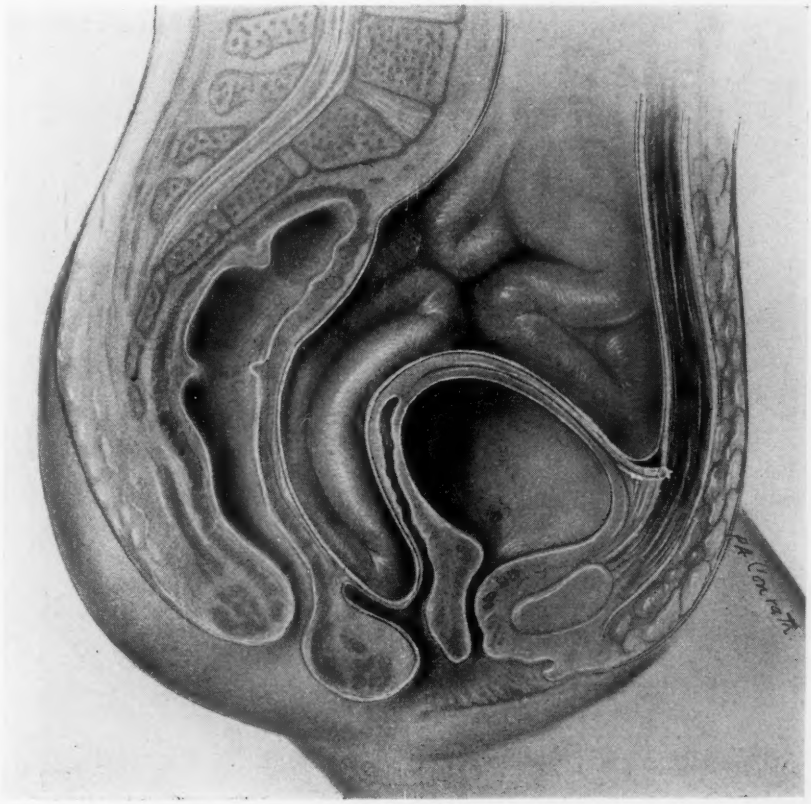


Fig. 4.—First patient, fifteen months after operation. Shows relationship of enterocele to rectum, perineal body, and vaginal introitus. Ventral fixation of vagina has resulted in marked stretching of posterior vaginal wall, causing elongation of cul-de-sac and vaginal herniation. Normal relationship of bladder and urethra to symphysis is maintained. Perineal body and rectovaginal septum are intact.

Rectus Suspension Principle of Crossed-Suspender Support

The ability of the vaginal walls to stretch when subjected to strain, tension, or pressure is well known. When ventral fixation of the vagina is employed as the *only* means of correcting bladder prolapse, the ability of this muscular tube to maintain permanently the bladder in normal position behind the symphysis is subject to question. If the vesicovaginal connective tissue septum is intact, in good condition, and can be included in the ventral fixation sutures, the prognosis is better than if the fascia is thin, atrophic, torn, and separated.

In our first patient, ventral fixation offered a poor prognosis. Therefore another kind of support was sought that would be readily available, strong, dependable, adequate, and permanent. At the same time it would have to be sufficiently flexible to permit normal bladder function and not interfere with the sex life of the individual. Moreover, it had to be applicable to the development of a technical sequence that would safeguard the patient, particularly from the standpoints of risk, trauma, and operating time.

The rectus suspension principle of crossed suspender support, for both the vagina and bladder (Figs. 9 and 12), has fulfilled all of these requirements in every patient on whom it has been used to date.

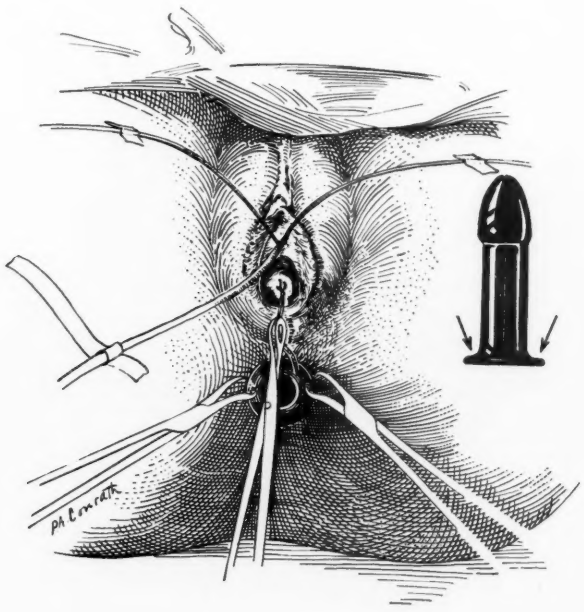


Fig. 5.—Preoperative preparation completed. Ureteral catheters in place. Bladder catheter connected with long tubing to permit distention during operation. Catgut suture in middle third of posterior vaginal wall is grasped with strong sponge forceps. Movement back and forth during closure of cul-de-sac facilitates accurate placement of purse-string sutures. Rectal dilator (inset) held in place with towel clips permits easy identification of relationships between rectum and surrounding structures. (Use of dilator suggested by Dr. A. P. Hudgins in a personal communication.

Technique

Preoperative Preparation.—

Special features (Fig. 5):

1. Both ureters are catheterized to facilitate identification and thus prevent injury during closure of cul-de-sac.

2. A medium-sized hard rubber rectal dilator (Fig. 5) is inserted to facilitate identification of extent and relationship of rectum to vagina, levator ani, lateral walls of pelvis, coccyx, sacrum, and blood vessels. It is held in place by two towel clips inserted through holes bored at 9 and 3 o'clock and clipped to the perianal skin.

3. A loop of No. 2 chromic catgut is placed in the middle one-third of the posterior vaginal wall. It is firmly grasped by a strong sponge forceps which is left in place during the operation. By having this instrument moved back and forth when placing sutures for cul-de-sac closure, accurate identification of relationship to pelvic floor, blood vessels, ureters, and rectum is greatly facilitated (Fig. 5).

4. A retention catheter is placed in the bladder and connected to long tubing so that the bladder may be distended and emptied, by an attendant, during the operation (Figs. 1 and 5). This is particularly helpful when separating the vagina from the bladder because accurate identification of the bladder wall and ureterovesical junctions is greatly enhanced. Trauma to the bladder is minimized. Moreover, proper application of the strips can be assured if the bladder is distended during this phase of the operation.

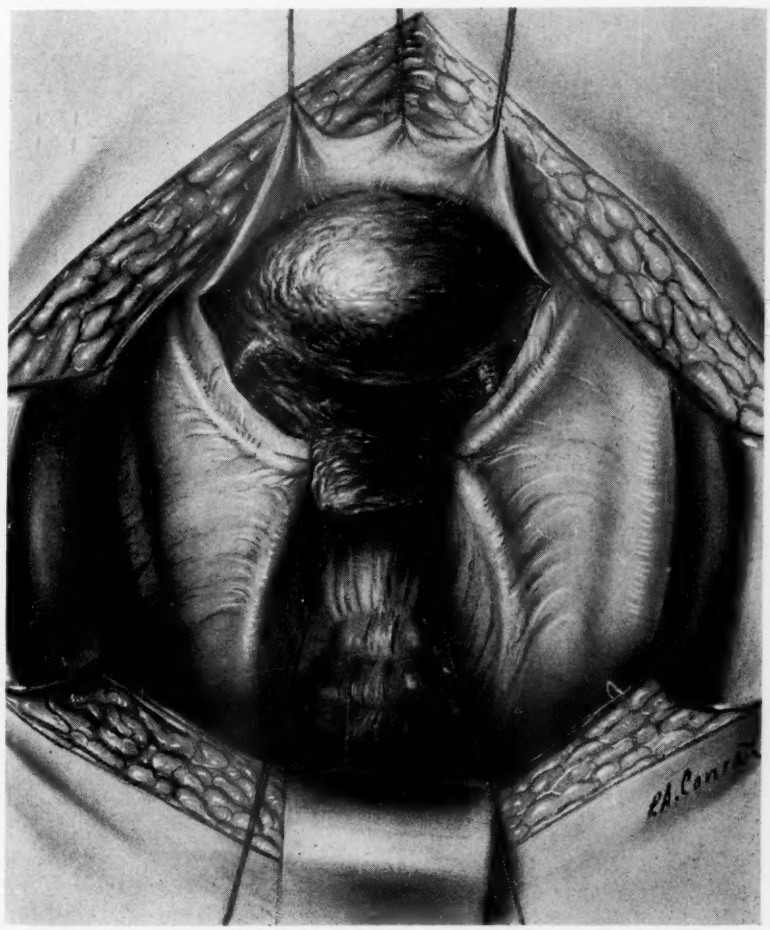


Fig. 6.—Traction sutures in peritoneal flap of bladder and cuff of vagina facilitate their separation down to level of ureterovesical junction on each side. Distention of bladder shows relationship to abdominal wall and vagina. Cul-de-sac is stretched and elongated.

Operative Procedure.—

The abdomen is opened through a midline subumbilical incision extending down to the symphysis. The intestines are packed off and the pelvis exposed.

Preparation of the vagina and bladder: The proximal end of the vagina is identified and pulled upward. The bladder peritoneum is reflected off the vaginal cuff or cervical stump, if present. Three traction sutures of heavy braided silk are placed in the peritoneal flap of the bladder. Two more are placed in the lateral limits of the vaginal cuff (Fig. 6). If the cervical stump is present it is circumcized and removed. The vaginal cuff is closed tight with chromic catgut before placing traction sutures. If ventral fixation is to be done, the cervical stump is not removed unless it is pathologic.

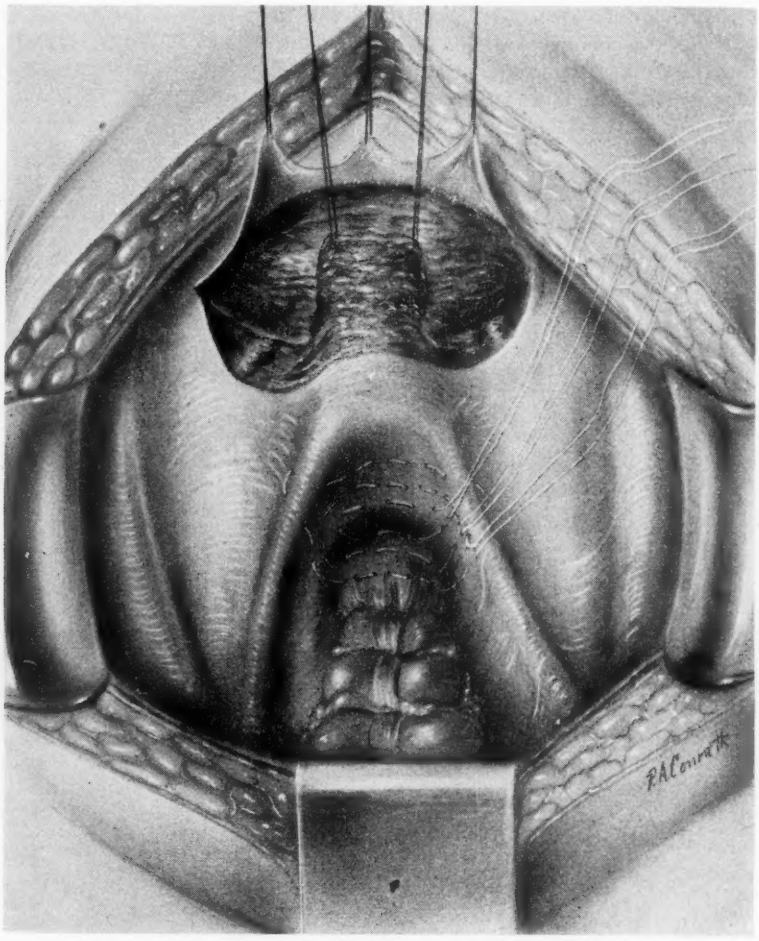


Fig. 7.—Closure of cul-de-sac below level of sacrouterine ligaments. Moschcowitz method of superimposed purse-string sutures which include posterior wall of vagina, rectum, and lateral pelvic walls. Each suture should be tied before the next one is placed.

Mobilization of the vagina and bladder: Traction on the bladder and vagina is applied in opposite directions and dissection is started. The anterior vaginal wall is separated from the bladder by blunt and sharp dissection down to the ureterovesical junction on each side. Trauma to the bladder wall is minimized as much as possible at the expense of increasing trauma to the vagina, if necessary. Intermittent distention of the bladder with antiseptic solution (1:2,000 aqueous Merthiolate) makes it possible to perform this part of the procedure with efficiency and dispatch. If the vaginal wall is accidentally

perforated a small drain may be inserted later or it can be closed with a simple through-and-through catgut suture. When the ureterovesical junction on each side is exposed, the bladder and vagina have been completely mobilized above the level of these landmarks (Fig. 6).

In the presence of scar tissue, bleeding is usually slight. If necessary it can be readily controlled with hot packs or a hemoplastic preparation.

We agree with Polk,[11] that extensive separation of bladder and ureters from the vagina causes far less hemorrhage than might be anticipated. He encountered moderate bleeding in only one of seventeen patients reported on. Bleeding was slight in all of the seven patients in our series.

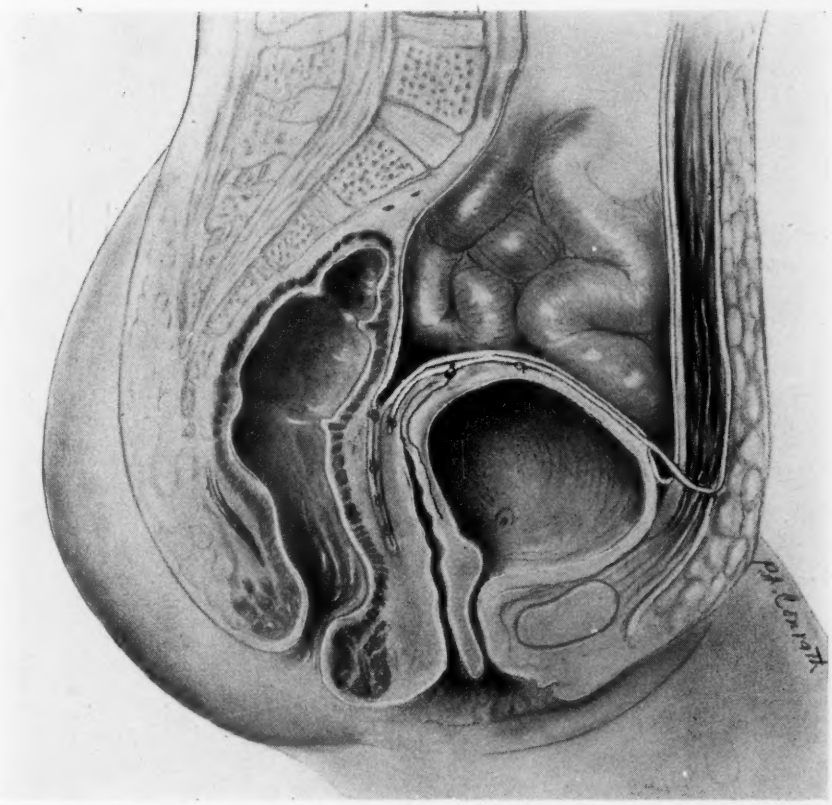


Fig. 8.—Vagina extends only short distance on to posterior bladder wall. Cul-de-sac closed below level of sacrouterine ligaments. "Crossed-suspender support" applied to bladder. Distal ends of strips sewed to posterior vaginal wall. Note separation of vagina from bladder down to level of ureterovesical junctions.

Closure of the cul-de-sac (Moschcowitz technique): After mobilization of the vagina and bladder, the cul-de-sac is closed. Moschcowitz,[6] in 1912, introduced a method of superimposed purse-string sutures between the vagina, rectum, and lateral pelvic walls, placed in such a manner as to cause complete obliteration of the cul-de-sac (Fig. 7). He used it successfully in the treatment of prolapse of the rectum. It is equally applicable when utilized for the prevention or correction of a posterior vaginal wall hernia.

Nonabsorbable sutures are employed for closure of the pouch below the level of the sacrouterine ligaments (Figs. 7 and 8). The lowermost suture is placed about one inch above the inferior extremity of the cul-de-sac. Similar

sutures, three to six in number, are passed through the peritoneum at intervals of 1 to 2 cm. until the level of the sacrouterine ligaments is reached. Each suture is tied before the next is placed. They pick up the peritoneum covering the posterior wall of the vagina, the lateral walls of the pelvis, and the anterior wall of the rectum. The folds of the sacrouterine ligaments are included in the uppermost suture (Fig. 7).

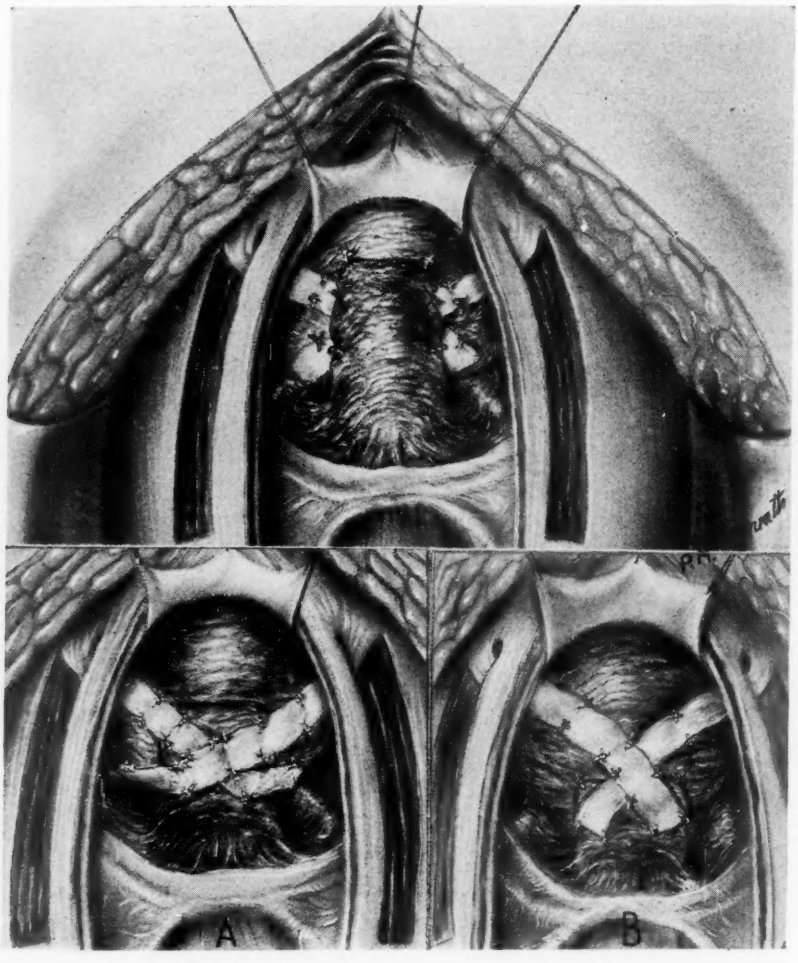


Fig. 9.—Vaginal vault sutured to strips after their attachment to bladder is completed. This method is applicable when vagina extends well up onto wall of distended bladder. It is to be preferred. When vagina extends only short distance onto posterior aspect of wall, it is included in distal ends of strips with "crossel-suspender support" applied to bladder (inset *B*). Strips may be crossed on posterior wall of vagina (inset *A*) when it extends between these two points; then ends are carried down to ureterovesical junctions and sewed to bladder.

When approaching the rectum, the sutures coming from the sides of the pelvis catch the serosal covering with firm, close stitches. This is done to prevent the possibility of subsequent intestinal herniation into the pouch through a defect between the walls of the rectum and pelvis. Two important structures must be avoided in placing these sutures: the ureters, which have been previously catheterized, and the internal iliac vessels, which can be readily identified by their pulsation.

This is a relatively simple procedure that requires about the same amount of time it would take to place an equal number of purse-string sutures elsewhere in the abdomen (Fig. 8).

Postoperative attention to bowels is the same as that employed in any other type of laparotomy.

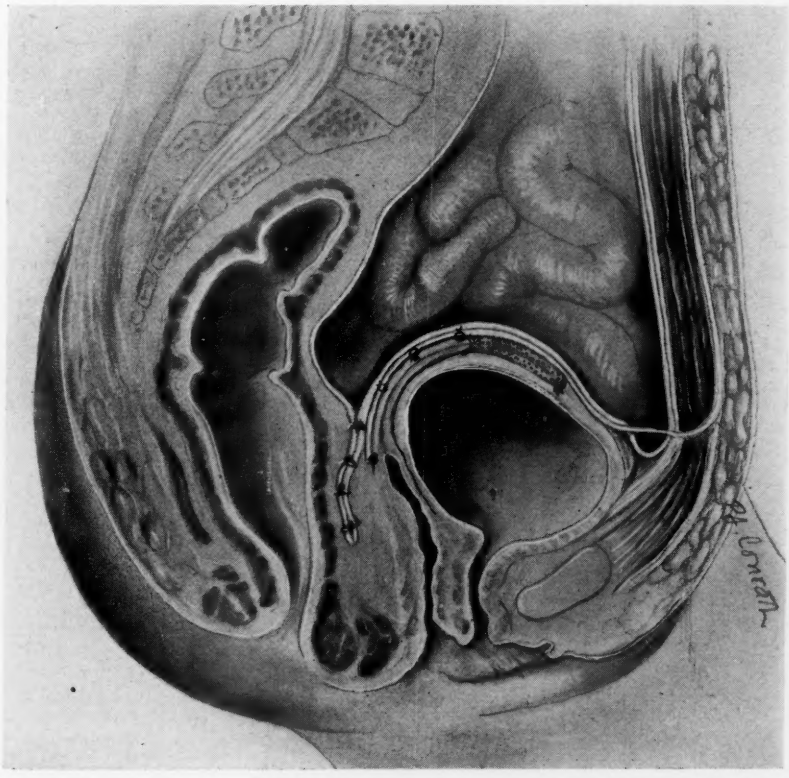


Fig. 10.—Vaginal vault is situated midway in relation to bladder; hence "support" is applied to posterior vaginal wall, and strip ends are sewed to bladder at level of ureterovesical junctions (not shown here).

Stippled area shows relationship of vagina when it extends well up onto bladder wall. Then it is sewed to strips after they have been applied to bladder (not shown here).

Criteria for determining the type of vaginal fixation to be used: After closure of the cul-de-sac, that part of the vagina situated above the level of the sacrouterine ligaments is still freely mobile. It may or may not be long enough to permit ventral fixation. This is determined before the next step in the operation is begun. If it extends only a short distance on to the posterior apsect of the distended bladder wall, it is included in the distal ends of the fascial strips, with the "crossed-suspender support" applied to the bladder (Figs. 8 and 9, inset *B*). If it extends well up onto the bladder wall, it is sutured to the strips after they have been attached to the bladder (Figs. 9, 10, stippled area, and 12). This seems to be the method of choice.

If the vaginal cuff is located between these two points, the "crossed-suspender support" may be applied to the posterior vaginal wall (Figs. 9, inset *A*, and 10), in which case the ends of the strips are sewed to the bladder if long enough (Fig. 9, inset *A*). Otherwise, they, too, remain in contact with the vagina. It is our impression that any one of these methods is preferable to

ventral fixation because the part of the vagina that is still unattached causes little or no additional strain to be placed upon the fascial supports. Moreover, if the vault is attached to the bladder musculature with one or two interrupted sutures of fine catgut, it does not interfere with normal function in any way (Fig. 9).

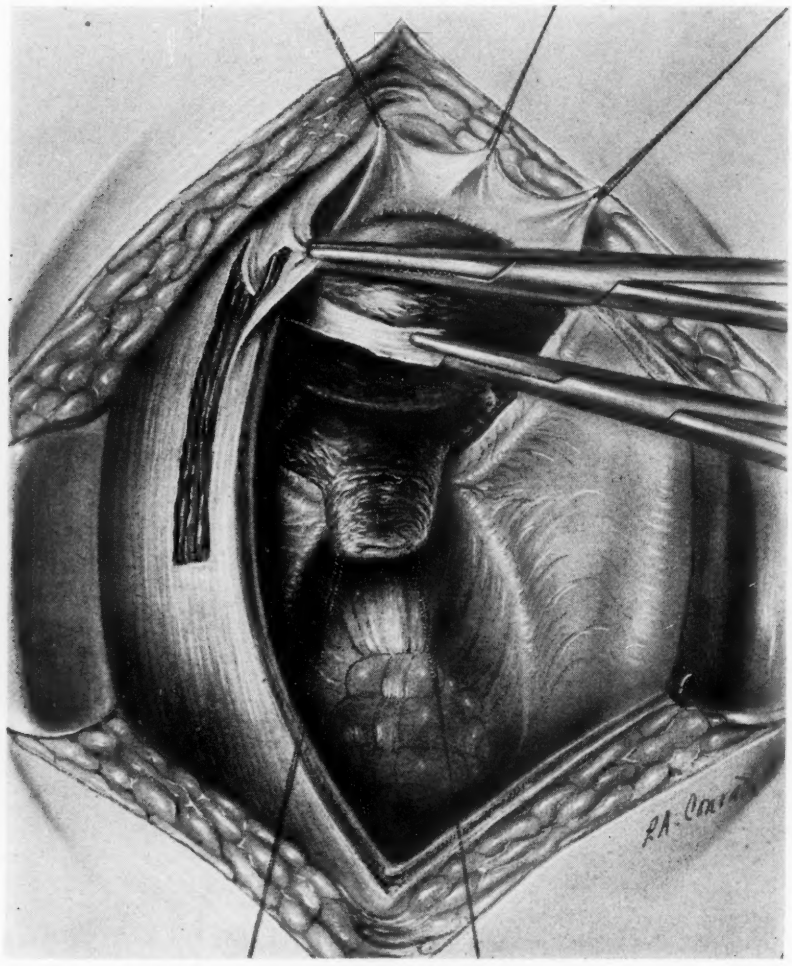


Fig. 11.—Fascial strip mobilized from anterior sheath of rectus is carried through muscle and parietal peritoneum down to ureterovesical junction on opposite side. Bladder is partially distended. Base of strip situated approximately 6 cm. above symphysis.

Mobilization and placement of the fascial strips: The anterior sheath of the rectus on one side is exposed. A fascial strip 1½ cm. in width, approximately 8 cm. in length, and situated 1½ cm. lateral to the cut edge of the fascia is mobilized in such a manner as to permit the base of the strip to be situated about 6 cm. above the symphysis pubis (Fig. 11). The strip must be long enough to reach the ureterovesical junction, *on the opposite side,* when the bladder is distended (Figs. 11 and 12). If the distal end is to be sutured to the vagina (Fig. 9, inset *B*) or the "crossed-suspender support" is to be applied to the posterior vaginal wall (Fig. 9, inset *A*), the strip should be long enough to

reach the level of the sacrouterine ligament *on the opposite side*. The strip may be lengthened or shortened by extending the base toward the symphysis with further incision or away from the symphysis by subsequent suture (Fig. 11). The base should be situated at or close to the point where the distending bladder first comes into contact with the anterior abdominal wall (Figs. 11 and 12).

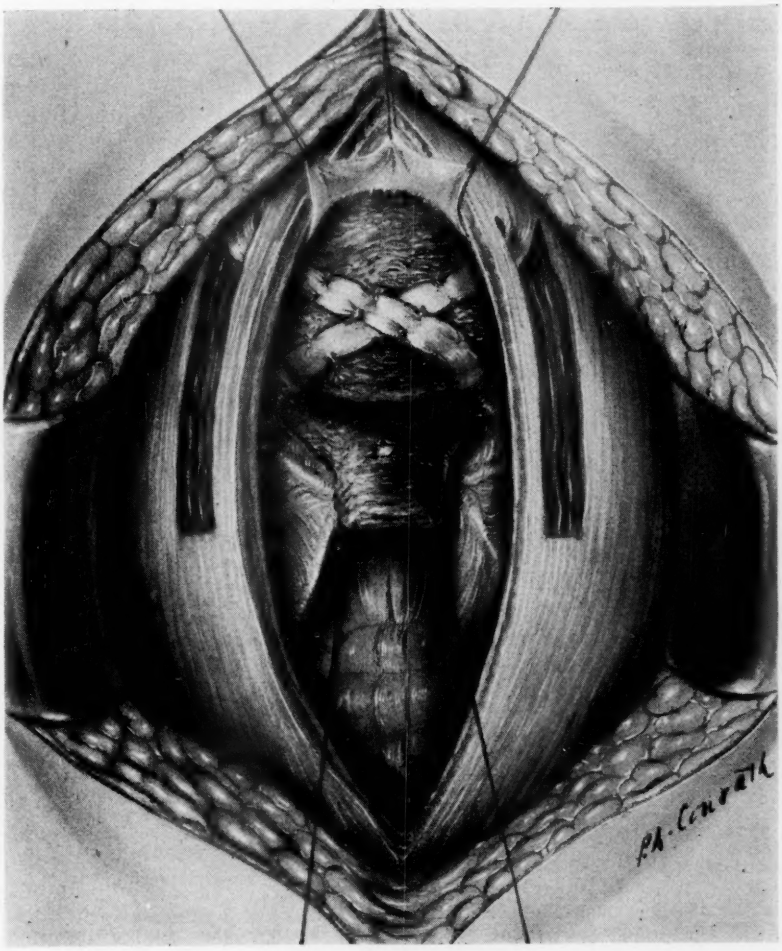


Fig. 12.—Shows "rectus suspension principle of crossed-suspender support." Strips are crossed as close to base of bladder as is conveniently possible. Relationship to bladder, as shown, is for purpose of demonstration. Ends of strips are in contact with, but not sutured to, ureters. Small rubber dam drain to vagina through accidental opening in wall.

The strip is carried directly through the muscle and parietal peritoneum and then down to the ureterovesical junction on the opposite side. When sutured in this position the distal end should be touching but not attached to the wall of the ureter. Interrupted sutures of fine nonabsorbable material, placed approximately 1 cm. apart, are used to attach the lateral borders of the strip to the muscular portion of the bladder wall (Fig. 12). Great care must be taken to be sure that the bladder mucosa is not included in any of these stitches. Partial distention of the bladder at this point is helpful. No. 34 alloy steel wire and fine linen have been used successfully. However, the choice of suture is a matter of individual preference so long as it is nonabsorbable.

After placement of the first strip is completed, the process is repeated on the opposite side in exactly the same manner. It is important to pay particular attention to two things:

First, the same degree on bladder distention must be maintained until both strips are in place, to be sure that subsequent bilateral support will be equalized (Fig. 12).

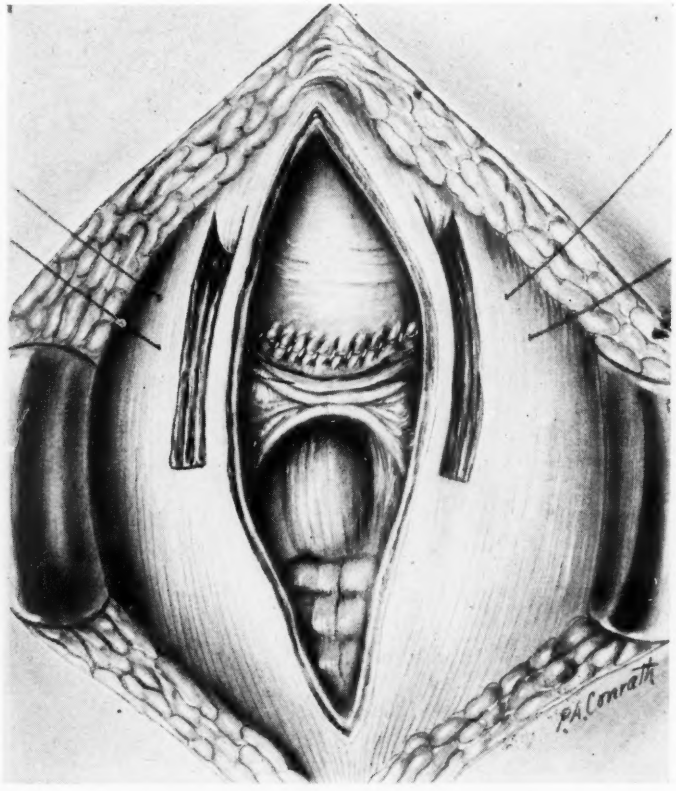


Fig. 13.—Peritonealization completed. Suture line shown here for purpose of illustration. Dome of bladder situated distal to bases of strips. Heavy silk sutures placed in anterior and posterior borders of cuff for ventral fixation of vagina.

Second, the location of the point at which the strips cross each other is decidedly important, because this is the point at which the greatest amount of support to the bladder is rendered. It should be situated on the inferior aspect of the bladder wall as close to the posterior border of the trigone as it is conveniently possible to get it. This is facilitated by taking the strips from the anterior sheaths of the fascia rather than from the medial borders. Although it causes the "crossed-suspender" effect to be rendered at a slightly wider angle, the point of greatest support to the bladder is more efficiently located. The possible theoretic increase in tension to which the bases of the strips may be subjected by their lateral relationship to the bladder is adequately compensated for by a more extensive distribution of support and by the fact that the degree of tension on the strips required to maintain normal visceral pelvic relationships is subject to wide variations, being directly influenced by changes in intra-abdominal pressure, differences in degrees of contraction and relaxation of both rectus muscles, and the amount of urine present in the bladder (Fig. 12).

Peritonealization: All raw surfaces are covered with bladder peritoneum. It is also sutured around the strips at the points where they penetrate the anterior parietal peritoneum (Fig. 12). The relationship of the bladder to the abdominal wall and adjacent strips is such as completely to obliterate any pockets into which loops of intestines might subsequently find their way (Fig. 13).

Technique of ventral fixation: If ventral fixation of the vagina is done, two heavy braided silk sutures are placed in the anterior and posterior borders of the vaginal vault or cervical stump and then brought out through the abdominal wall lateral to the defects in the rectus sheaths (Fig. 13). They are tied on each side and then crossed and tied in midline before closure of the skin and subcutaneous tissue (Fig. 14).

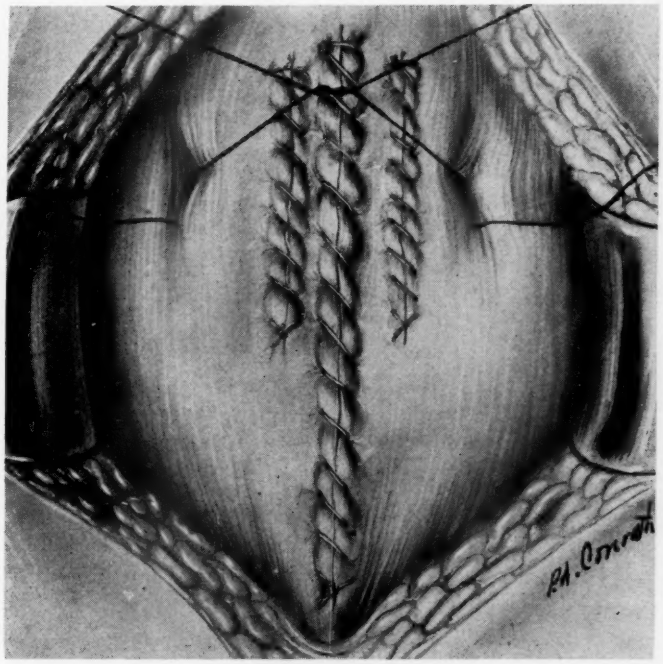


Fig. 14.—Strip defects closed with continuous catgut. Fascia closed with interrupted nonabsorbable sutures (not shown here), preferably cotton or wire, to safeguard against subsequent development of incisional hernia. Ventral fixation sutures are tied on each side (not shown here) and then crossed and tied in midline before closure of skin and subcutaneous tissue.

Closure of the abdomen and fascial defects: When the vagina is attached to the fascial strips, the peritoneum is closed in the usual manner without drainage. The defects in the rectus sheaths are closed with continuous chromic catgut. The fascia is closed with interrupted nonabsorbable sutures, preferably cotton or wire, as an additional safeguard against incisional hernia later on. Catgut may be used to approximate the sheath defects because they are protected by the underlying muscles (Fig. 14).

Postoperative Treatment.—Postoperative treatment is routine except that continuous bladder drainage is maintained for at least six days. When discontinued, careful precautions must be taken to be sure that subsequent overdistention does not occur. Most patients are able to void after the seventh day. Then a check is made for residual urine every twelve to twenty-four hours,

depending upon the fluid intake and output, until the amount obtained is less than 100 cubic centimeters. Routine catheterization technique is used. When it is no longer necessary, the patient is advised to empty the bladder every six hours or just as soon as she begins to notice a slight pressure or discomfort in this region.

Discussion

1. The first patient in this series had developed an enterocele fifteen months after operation. Two small incisional hernias were noted six and one-half years later, but the defects in the anterior rectus sheaths were intact. She was taken to the operating room again. At this time the enterocele, which had now been present for almost six years, was corrected by obliteration of the cul-de-sac. The bladder was still situated snugly behind the symphysis. The vagina had become intimately incorporated into the bladder wall by adhesions so dense that identification of the upper third was almost impossible. The fascial strips were intact and functioning. They were not stretched or elongated. On the contrary, they had been reinforced considerably by fibrous bands of postoperative adhesions between the anterior abdominal wall and that part of the superior wall of the bladder that was immediately adjacent. The strip on the left was difficult to identify because of the density of the adhesions. It would have been impossible to displace the bladder had we wanted to. The anterior wall and dome of the bladder were in normal position in relation to the pubovesical space and the lower abdominal wall.

2. We now prefer to suture the vagina to the fascial strips, whenever possible (Fig. 9). The "crossed-suspender support" can thus be applied more effectively to the base of the bladder and the ureteral junctions (Fig. 12) than when it or the ends of the strips are attached to the posterior wall of the vagina (Figs. 9, insets *A* and *B*). After suspension of the bladder is completed, the anterior wall and cuff of the vagina are sutured to the posterior aspects of each strip with interrupted catgut sutures (Fig. 9). If additional fastening seems advisable, the vault may be stitched to the bladder musculature, using one or two interrupted sutures of fine catgut (Fig. 9). This was done on one of our patients in whom bladder function was not affected.

3. Ventral fixation of the vagina was performed on the first patient because the tube was long, thin, and relaxed (Fig. 4). Moreover, it was decided to minimize the pull on the strips until a period of observation would permit consideration of the advisability of increasing their load with that part of the vagina situated above the level of the sacrouterine ligaments. Obliteration of the cul-de-sac was not done on this patient until six years later (Figs. 2 and 4).

After fifteen months of observation, during which time the fascial strips were apparently unaffected by prolonged periods of increased strain and pressure, it was decided to employ the same principle again with modifications (Fig. 9).

4. Obliteration of the cul-de-sac (Fig. 7) was considered essential in the second patient because the first patient had acquired a well-developed posterior vaginal wall hernia (enterocele) fifteen months after operation (Fig. 4). She

had no rectocele because a colpoperineal repair had been performed when the uterus was removed and she still had a good result (Figs. 2 and 4). The second patient had a small rectocele but no enterocele; therefore, a colpoperineorrhaphy was done first under local infiltration anesthesia. Then the abdomen was opened under general anesthesia and the operation herein described was performed (Figs. 12 and 9), including obliteration of the peritoneal pouch of Douglas (Figs. 7 and 8).

5. Approximately six years have elapsed since the second operation, during which time this principle has been used in five additional cases. In one patient the distal ends of the fascial strips were approximated to the vagina after the "crossed-suspender support" had been applied to the bladder (Fig. 9, inset *B*). In another the "support" was applied to the posterior vaginal wall while the ends of the strips were carried down to the ureterovesical junctions and sewed to the adjacent bladder musculature (Fig. 9, inset *A*). In the other three the vagina was sewed to the fascia and bladder musculature (Fig. 9) after vesical application of the "support" and strips (Fig. 12). We now have four cases in this latter category, one of each in the second (Fig. 10, insets *A* and *B*), and one, the first, in the ventral fixation group (Figs. 4, 13, and 14).

6. Because we appreciate the fallibility of any operation for vaginal prolapse that has not been subjected to long periods of follow-up observation, we have refrained from previous publication of this method. We do so now, only with the hope that it will be used by others who will help to discover its defects. We agree with Miller,[13] that "in all new and untried procedures there are faults to overcome and minor difficulties to be ironed out."

7. The operation was performed for the first time over seven years ago. To date we have a series of seven patients in whom this principle has been used for the treament of complete prolapse of the vagina and bladder following hysterectomy.

Summary

Seven Cases Are Available to Date.—

CASE 1.—Operation, 1940. Support to bladder. Ventral fixation of vagina (Figs. 12 and 13). Posterior vaginal wall hernia developed fifteen months later (Fig. 4). Two small incisional hernias discovered six years later. Otherwise result good (Fig. 2).

Second operation, 1947. Closure of cul-de-sac for treatment of enterocele. Repair of incisional hernias. Result good to date.

CASE 2.—Operation, 1941. Support to bladder. Vagina sewed to strips. Cul-de-sac closed (Fig. 9). Still being observed. Result good to date.

CASE 3.*—J. B. Operation, 1942. Support to bladder. Strip ends to posterior vaginal wall (Fig. 9, inset *B*). Cul-de-sac closed. Result good after nine months. No contact since.

CASE 4.*—R. G. H. Operation, 1943. Support to bladder. Vagina sewed to strips (Fig. 9). Cul-de-sac closed. Good result after three months.

Contact re-established three years later. Result still good to date.

CASE 5.*—R. G. H. Operation, 1943. Support to vagina. Strip ends to bladder. (Fig. 9, Inset *A*.) Result good after 3 months. No contact since.

CASE 6.*—M. F. Operation, 1944. Support to bladder. Vagina to strips (Fig. 9). Cul-de-sac closed. Good result after four months. No contact since.

CASE 7.—Operation, 1946. Support to bladder. Vagina to strips (Fig. 9). Cul-de-sac closed. Still being observed. Result good to date.

*Performed while in the A.A.F. Armed Services.

Conclusions

Additional cases and longer periods of observation will be necessary before conclusive evidence can be substantiated.

The author wishes to express his gratitude and appreciation to Mr. Philip A. Conrath, Art Department, St. Louis University School of Medicine, for his excellent work in preparing the illustrations contained herein.

References

1. Demarest, D.: Am. J. Surg. **34**: 285-289, 1920.
2. Palsey, C. B.: Brit. M. J. **1**: 102, 1920.
3. Hepburn, T. N.: Surg., Gynec. & Obst. **44**: 400, 1927.
4. Phaneuf, L. D.: Surg., Gynec. & Obst. **77**: 209-215, 1943.
5. Marion, A.: Rev. gyn. chir. abdom., Paris **13**: 465, 1909.
6. Moschcowitz, A. V.: Surg., Gynec. & Obst. **15**: 7-21, 1912.
7. Ward, George Gray: J. A. M. A. **69**: 709-713, 1922.
8. Mella, C. A., and McClelland, G. S.: Urol. & Cutan. Rev. **47**: 157-160, 1943.
9. Walscheid, A. J.: J. M. Soc. New Jersey **39**: 274-279, 1942.
10. LeTinde, R. W.: J. A. M. A. **127**: 495-502, 1945.
11. Polk, W. M.: Surg., Gynec. & Obst. **15**: 322-333, 1922.
12. Berkely, C., and Bonney, V.: Gynecological Surgery, New York, Paul B. Hoeber, Inc.
13. Miller, N. F.: Surg., Gynec. & Obst. **44**: 550-555, 1927.
14. Brady, L.: Am. J. Obst. & Gynec. **32**: 295-299, 1936.
15. Ward, G. E.: Arch. Surg. **36**: 163-170, 1938.

634 N. Grand Avenue.

Discussion

DR. NORMAN F. MILLER, Ann Arbor, Mich.—Dr. Fletcher has described and offered for our consideration a new operation for the correction of complete inversion of the vagina and its concomitant cystocele following hysterectomy. Theer are a number of operations for the correction of this condition such as ventrofixation, LeFort colpocleisis, correction of the cystocele enterocele, plus vaginopexy, none of which is entirely satisfactory. Although I have not used Dr. Fletcher's technique I am impressed by his reported results and the potentialities of his operation.

Since muscle is a basic element in support, it is odd that vaginal inversion should occur, even though rarely, if, during hysterectomy, the musculofascial paravaginal tissues, the cardinal, round, and sacrouterine ligaments, are called upon to give support to the remaining cervix or vaginal apex. Perhaps failure to use these structures accouns for the occasional vaginal inversion encountered. Whatever its etiology, however, the condition does occur and Dr. Fletcher has advocated the use of fascial strips taken from the rectus sheath as a means of providing support for the bladder and vagina.

In the past the use of fascia has not played a prominent part in the correction of gynecologic conditions. Perhaps we have overlooked a useful source of support with which we may achieve permanent relief for some of the gynecologic relaxations. The use of fascia in the management of urinary incontinence represents one application and now this operation gives us another field of fascial usefulness. Just how long transplanted fascia continues functional remains to be determined. Dr. Fletcher's observations in this connection have been favorable. Others have reported permanence of transplanted fascia. My own experience in this connection has not convinced me of its durability. In several patients treated for urinary incontinence by means of fascial transplant, I have failed to find the fascial strips some years later at the time of reoperation for the original symptom. Doubtless, time and further experience will answer this question.

Dr. Fletcher has emphasized the importance of differentiating between rectocele and enterocele in patients with inversion of the vagina. The desirability of eliminating the cul-de-sac of Douglas at the time of operation also seems entirely logical and sound.

It is interesting to note that in spite of the fact that this operation is primarily a bladder support, no disturbance of bladder function is reported.

In studying the diagrams of the operation I am not convinced that the excellent drawings correctly illustrate the final result. Thus, if Fig. 4 illustrating the result fifteen months after operation actually portrays the end result, then I fail to see how or why the vagina or bladder are supported. Collapse of the bladder in Fig. 4 would seem to permit descent of bladder, vagina, and cul-de-sac. Since Dr. Fletcher's results with this operation have been satisfying to him, I take it Fig. 4 does not correctly illustrate the postoperative relationships.

In his present technique Dr. Fletcher uses fascial strips from the rectus sheath approximately 3 cm. apart. Fascial strips taken much further apart, as from the external oblique, or, more easily, as a transplanted strip of fascia lata, would, it appears to me, make for vastly better support. Thus, a strip of fascia lata extending from one internal inguinal ring to the other paralleling the subperitoneal course of the round ligaments would provide good support and offer the added advantage of permitting an entirely normal direction to the supported vagina without the possibility of interfering with bladder function. I hope Dr. Fletcher will consider this variation in some of his future cases.

To me this has been an interesting report and the author deserves much credit for his originality in conceiving the technique and for his restraint in waiting seven years for reasonable proof of adequacy before recommending it for our consideration.

DR. FLETCHER (Closing).—Obviously, the drawings were made primarily to illustrate the principle involved. To do this it was not possible to include all technical details in some of the pictures. For instance, the "crossed-suspender support" is shown situated higher up on the bladder than it actually is when the bladder is not distended.

Four of the patients in this series are still being observed. One was followed for three months, another for six months. A third was seen three months after operation and then lost. Contact was re-established three years later. She still has a good result from the operation performed in 1942.

The extent to which the procedure can be accurately evaluated still has to be established. We are trying not to be too enthusiastic. We do not see this type of case very often, but eventually we hope to have the opportunity to accumulate a sufficient number of patients to warrant careful evaluation of the principle of "crossed-suspender support" for what it is actually worth or not worth.

CESAREAN SECTION IN DETROIT DURING 1945—A COMPARISON WITH 1925 AND 1930*

HAROLD C. MACK, M.D., AND R. S. SIDDALL, M.D., DETROIT, MICH.
(From Wayne University College of Medicine)

PREVIOUS studies of the cesarean sections performed in Detroit which were made by Welz[1] and Seeley[2] for the years 1925 and 1930, respectively, showed a marked reduction in mortality during the intervening five years. In view of the steady decline in maternal mortality and the great improvement in the results of surgery in recent years, an analysis was made of cesarean sections performed during 1945, to determine the results of abdominal delivery in this city as compared to fifteen and twenty years ago. It was hoped that such a study would throw light on the means for further improvement.

In Detroit there were 36,100 live births for the year 1945, 32,634 during 1930, and 32,054 in 1925. As seen in Table I, there was a marked increase in the proportion of hospital deliveries during the twenty years. This change should be taken into account later when the comparative incidence of cesarean section for the individual hospitals in the different periods is considered. Table I also shows the deaths for the three periods, with noteworthy reduction in both maternal and infant mortality rates.

TABLE I

	1925	1930	1945
Live births	32,054	32,364	36,100
Total births	33,416	34,007	37,028
Birth rate	25.7	20.6	21.4
Births in hospitals	32.2%	44.5%	94.3%
Maternal deaths	219	215	58
Maternal death rate (per 1000 live births)	6.8	6.6	1.6
Infant death rate (per 1,000, under one year)	80.1	64.7	33.6
Cesarean sections	154	203	1,000
Frequency	1 in 217	1 in 167	1 in 37
Maternal deaths	20 (13%)	9 (4.4%)	8 (0.8%)
Infant deaths	17 (11%)	26 (12.8%)	78 (7.8%)

In the same Table I are given the actual numbers of cesarean sections for the years 1925, 1930, and 1945, as well as the frequency among the total number of births which these figures represent. It will be noted that this frequency had so increased that, by 1945, cesarean section was employed nearly six times as often as in 1925. It is equally remarkable, however, that the mortality rate of the operation in 1945 was only one-sixteenth that of 1925, and less than one-fifth of that in 1930. Actually, the 1945 death rate for abdominal delivery was

*Read before the Central Association of Obstetricians and Gynecologists on Oct. 25, 1947, in Louisville, Ky.

only slightly greater than the official maternal death rate fifteen and twenty years before. However, due to the great reduction in the general maternal risk, it is still five times the over-all maternal mortality for 1945. On the other hand, the infant death rate for cesarean section showed only moderate reduction. These differences will be subjected to further analysis later.

Table II shows the variations in the incidence of cesarean sections for the hospitals with 1,000 or more deliveries in 1945. There is also an interesting comparison with the figures, where available, from the reports of Welz and Seeley. The rather general tendency toward an increase reflects the trend for the city as a whole.

TABLE II. CESAREAN SECTION INCIDENCE IN LARGER HOSPITALS (1,000 OR MORE DELIVERIES)

HOSPITAL CODE NO.*	1925 (WELZ)	1930 (SEELEY)	1945
16	1 in 206	1 in 203	1 in 78 (1.2%)
6	1 in 62	-------	1 in 75 (1.3%)
12	1 in 142	1 in 247	1 in 70 (1.4%)
4	1 in 73	1 in 93	1 in 65 (1.5%)
3	1 in 471	1 in 160	1 in 47 (2.1%)
7	1 in 97	1 in 63	1 in 45 (2.1%)
15	-------	-------	1 in 40 (2.4%)
19	1 in 24	1 in 74	1 in 37 (2.7%)
9	1 in 30	1 in 32	1 in 34 (2.9%)
17	-------	-------	1 in 34 (2.9%)
8A	-------	-------	1 in 28 (3.5%)
18	1 in 34	1 in 34	1 in 27 (3.7%)
8	1 in 31	1 in 52	1 in 21 (4.6%)
21	1 in 206	1 in 45	1 in 13 (7.4%)

*Official Code Number, Detroit Department of Health.

In Table III are shown the incidences of the different types of abdominal delivery with their mortality rates where available. The superiority of the low cervical operation over the classical type seems to be rather clearly demonstrated in 1945 as in the previous studies.

TABLE III. TYPES OF CESAREAN SECTION

	INCIDENCE	MORTALITY		
	1945	1925	1930	1945
Classical	350 (35.0%)	13.3%	7.6%	6 (1.71%)
Low cervical	586 (58.9%)	9.0%	0.0%	2 (0.34%)
Cesarean-hysterectomy	28 (2.8%)	-----	9.0%	0
Extraperitoneal	12 (1.2%)	-----	-----	0
Unknown	21 (2.1%)	-----	-----	0

In Table IV the hospitals are listed according to the number of deliveries in 1945 as follows: 2,000 or more; 1,000 to 1,999; and less than 1,000. Interesting and, in some instances, significant are the data concerning the general maternal mortality rate, the incidence of cesarean section, and the mortality with abdominal delivery in the different classifications. In the two groups consisting of the larger maternity hospitals the results are quite comparable and are defi-

nitely superior to those of the smaller hospitals. For the latter, however, it should be noted that the maternal mortality would appear as 2.6 per 1,000 live births if Detroit Receiving Hospital (No. 40) were eliminated. This seems justifiable since Receiving has no maternity service, and only extremely ill, or otherwise untransferable, emergency obstetric cases are admitted. Moreover,

TABLE IV. INCIDENCE OF CESAREAN SECTION, GENERAL MATERNAL MORTALITY, AND CESAREAN SECTION MORTALITY ACCORDING TO SIZE OF MATERNITY SERVICE

HOSPITAL CODE NO.*	LIVE BIRTHS	MATERNAL DEATHS	CESAREAN SECTIONS		
			NUMBER	PERCENTAGE	DEATHS
A. *2,000 or more births* (Maternal death rate: 1.1 per 1,000 live births)					
8	2,021	0	94	4.6	0
9	2,274	2	66	2.9	0
21	2,953	1	219	7.4	1
16	3,130	7	40	1.2	1
15	3,619	6	90	2.4	0
Total	13,997	16	509	3.6	2 (0.39%)
B. *1,000 to 1999 births* (Maternal death rate: 1.1 per 1,000 live births)					
17	1,099	2	32	2.9	2
6	1,206	2	16	1.3	0
12	1,271	4	18	1.4	0
3	1,327	1	28	2.1	0
4	1,431	1	22	1.5	0
7	1,554	0	34	2.1	0
18	1,683	0	61	3.6	0
19	1,739	2	47	2.7	0
8A	1,820	2	65	3.5	0
Total	13,130	14	323	2.5	2 (0.62%)
C. *Less than 1,000 births* (Maternal death rate: 3.46 per 1,000 live births)					
35	1	0	0	0.0	0
40A	1	0	0	0.0	0
34	12	0	2	16.6	0
38	14	0	0	0.0	0
36	16	0	1	6.4	0
31	20	0	9	45.0	0
40	33	6	0	0.0	0
41	43	0	0	0.0	0
29	60	0	1	1.6	0
37	67	0	0	0.0	0
22	130	1	7	5.3	0
33	161	1	4	2.4	0
25	272	1	2	0.7	0
24	326	1	18	5.5	0
11	329	2	30	9.1	0
23	382	0	6	1.6	0
39	389	2	2	0.5	1
14	420	1	12	2.8	1
20	492	2	5	1.0	0
2	497	1	48	9.6	1
26	552	1	3	0.54	0
5	554	0	5	0.9	0
13	612	1	8	1.3	1
27	712	4	1	0.14	0
1	851	0	4	0.47	0
Total	6,946	24	168	2.4	4 (2.38%)
D. *Home deliveries* (Maternal death rate: 2.0 per 1000 live births)					
	2,027	4	0	0.0	0
Grand Total	36,100	58	1,000	2.77	8 (0.8%)

*Official Code Number, Detroit Department of Health.

the large number of serious abortion and ectopic pregnancy cases admitted accounts for deaths which are not truly obstetric but nevertheless (according to Department of Health statistics) are counted in the maternal mortality. On the other hand, we found no defense for the fact that three of the four cesarean fatalities ascribable in whole or in part to questionable indications or treatment occurred in these small hospitals. It is significant to note that only 9 (36 per cent) of the 25 smaller hospitals conformed to the standards of the American College of Surgeons. The importance of proper standards for maternity care is shown by the fact that the mortality rate for cesarean section for all 23 approved hospitals, regardless of their size, was 0.56 per cent for 887 abdominal sections, whereas the death rate for those not approved was 2.65 per cent. In other words, 37.5 per cent of all cesarean deaths for the entire city occurred in the 16 small, substandard institutions where only 11.3 per cent of all cesarean sections and 13.3 per cent of all deliveries took place!

TABLE V. INDICATIONS AS GIVEN FOR CESAREAN SECTIONS IN 1945

Cephalopelvic disproportion		261	Malpresentation, malposition		21
Repeat sections		166	Transverse	5	
Hemorrhage		164	Brow	1	
Placenta previa	109		Face	3	
Abruptio placentae	55		Breech	6	
Contracted pelvis		123	Transverse arrest	3	
Gen. contracted		71	Undefined	3	
Flat		6	Fetal indications		7
Funnel		13	"Fetal distress"	3	
Fractured		1	Monstrosity	1	
"Subluxation"	1		Hydrocephalus	1	
Unclassified	31		Triplets + intestinal obstruction	1	
Toxemia		73	Prolapsed cord	1	
Eclampsia	18		Ruptured uterus		2
Pre-eclampsia	15		Abdominal pregnancy		1
Nephritic	3		Miscellaneous		51
Hypertensive	1		Elderly primipara	21	
Unclassified	36		Previous stillbirth	6	
Dystocia		46	Diabetes	5	
"Prolonged labor"	10		Arrested tuberculosis	4	
Inertia	14		Hyperthyroidism + heart disease	1	
Contraction ring	2		Psychoneurosis	1	
"Rigid cervix"	2		Postpolio, paralysis	1	
"Pelvic dystocia"	18		"Spastic condition"	1	
Conditions of perineum, vulva, vagina, cervix, uterus		30	"Bleeding tendency"	1	
Previous plastic	13		Gangrene mesenteric gland	1	
Previous myomectomy	2		"Kidney infection"	1	
Double uterus	2		Pulmonary carcinoma	1	
Double vagina	1		Rh negative	4	
Stenosis of cervix	4		Heart disease	2	
Rectovaginal fistula	3		Multiple sclerosis	1	
Atresia, vaginal	2				
Prolapse	1				
Infected perineum	1				
Condylomata	1				
Pelvic tumors		22			
Uterine fibroids	16				
Ovarian cyst	4				
Undefined	2				
Unknown					33
Charts missing		21			
"Elective"		12			

(2 postmortem cesarean sections not included)

The indications, as given for the 1,000 sections performed in 1945, are classified in Table V. The validity of the indications could not be subjected to close scrutiny since, in most instances, the data were furnished by the hospitals; and, where data were obtained by us from personal inspection of hospital records, salient features establishing the diagnosis and indications were at times lacking.

Notwithstanding evident extension of indications over former years, to include such new entities as "Rh negative," a comparison of the major reasons for cesarean section with those given in 1925 and 1930 shows less proportional variation than had been anticipated. This comparison is given in Table VI.

TABLE VI

	1925	1930	1945
Cephalopelvic disproportion (including contracted pelvis and dystocia)	48 (31%)	85 (42%)	430 (43%)
Repeat section	27 (18%)	34 (17%)	166 (17%)
Hemorrhage (placenta previa, abruptio)	17 (11%)	25 (12%)	164 (16%)
Toxemia	26 (17%)	16 (8%)	73 (7%)
All others	36 (23%)	43 (21%)	167 (17%)

In each of the three series, "cephalopelvic disproportion" (including the various types of "contracted pelvis," whether or not proved by adequate test of labor or pelvimetry) was the most common reason for section, representing 31, 42, and 43 per cent, respectively. The steady increase in frequency of this indication suggests a growing tendency to resort to early section in instances of actual or suspected dystocia. In spite of the growing use of sections, the proportion of cases subjected to "Repeat section" remains at a surprisingly constant level of 18, 17, and 17 per cent, respectively. In 1925, toxemia (including eclampsia, pre-eclampsia, and cardiovascular-renal disease) was the third most frequent indication (17 per cent), whereas in 1930 and 1945 this indication had dropped to fourth place with 8 and 7 per cent each. In 1925 and 1930, hemorrhage (placenta previa and premature placental separation) accounted for 11 and 12 per cent of all sections. In 1945 this indication had risen slightly to 16 per cent of all sections. Miscellaneous reasons comprised 23, 21, and 17 per cent.

While some proportional differences among the major indications for cesarean section are noted since 1925, it is evident that a numerical increase in sections for all causes took place in 1945. Table VII shows a surprising uniformity in the practice of the three hospital groups (classified according to size) with respect to cesarean section for "cephalopelvic disproportion." The greater fre-

TABLE VII. INDICATIONS ACCORDING TO SIZE OF HOSPITALS

	2,000 OR MORE BIRTHS	1,000 TO 1,999 BIRTHS	LESS THAN 1,000 BIRTHS
Cephalopelvic disproportion (including contracted pelvis and dystocia)	219 (43.0%)	139 (43.0%)	73 (43.4%)
Repeat section	98 (19.2%)	63 (19.5%)	6 (3.6%)
Hemorrhage	83 (16.3%)	61 (18.8%)	21 (12.5%)
Toxemia	28 (5.5%)	25 (7.7%)	19 (11.3%)
All others	81 (15.9%)	35 (10.8%)	49 (29.2%)

quency of "Repeat section" in the two larger groups of maternity services suggests that such cases drift to the hands of specialists. On the other hand, the greater proportion of sections for "hemorrhage" in the larger hospitals and the greater percentage of sections for "toxemia" and miscellaneous causes in the smaller ones may indicate some differences in attitude toward the management of these complications.

Most striking in the several contrasting features of the three time periods is the phenomenal reduction in the cesarean death rate. In 1925 there was an appalling maternal mortality of 13 per cent, which in 1930 fell to 4.4, and in 1945 to 0.8 per cent. The 8 maternal deaths of 1945 and their salient clinical features are summarized below:

1. Primipara, white, aged 24 years. Pregnancy near term complicated by massive edema of the vulva and lower extremities; 30 pound weight gain; hypertension and albuminuria. No improvement after intensive medical treatment in the hospital for seven days. Low servical cesarean section under spinal anesthesia was followed by immediate postoperative shock. Death occurred in one hour and forty-five minutes despite blood transfusion, glucose, plasma, etc. Premature fetus, weighing 3 pounds, 10 ounces, survived. Autopsy: marked anasarca, focal liver necrosis, hemorrhage in abdomen. Cause of death: severe, fulminating pre-eclampsia with postoperative shock.

2. Primipara, white, aged 27 years. Pregnancy at seven months was complicated by headache, dyspnea, edema, albuminuria, and mild phlebitis. There was no improvement under medical management in the hospital during three weeks. Blood pressure rose from 154/90 to 212/140. Low cervical cesarean section under general anesthesia. Premature infant died in twenty-four hours of pulmonary atelectasis. Good postoperative recovery with fall of blood pressure to 134/100. Death from pulmonary embolism on sixteenth day following discharge from hospital. Cause of death: pulmonary embolism.

3. Primipara, white, aged 29 years. Classical cesarean section twenty-four hours after rupture of membranes and prolonged labor associated with unrecognized face presentation. Peritonitis and adynamic ileus evident before operation. Infant weighed 8½ pounds; lived. Death on fifth postoperative day from peritonitis, despite intestinal intubation, penicillin, oxygen, etc. Cause of death: peritonitis.

4. Multipara, Negro, aged 32 years. Entered hospital at term with severe bleeding which continued for twenty-four hours and resulted in shock. Classical cesarean section was performed under general anesthesia while in shock. Death occurred at conclusion of operation. Uterus filled with blood; fetus stillborn. Inadequate preoperative transfusion; 250 c.c. blood, 1,000 c.c. plasma, 500 c.c. glucose given during operation. Cause of death: probable premature separation of the placenta with exsanguination.

5. Primipara, Negro, aged 27 years. Normal pregnancy at term. Hospital chart could not be found. Attending physician stated that "nausea, vomiting and exhaustion" ensued after labor of thirty-six hours. Classical cesarean section was performed under spinal anesthesia. Death occurred on fourth postoperative day. Cause of death unknown.

6. Primipara, white, aged 20 years. Normal pregnancy. Classical cesarean section five hours after admission to hospital with ruptured membranes in active labor. Section indicated by "lack of progress." No evidence of pelvic contraction or disproportion. Infant weighed 7 pounds; lived. Rising postoperative temperature despite penicillin, blood transfusions, etc. Death on tenth postoperative day from peritonitis, septicemia, and wound infection. Autopsy: generalized peritonitis; necrosis of endometrium.

7. Multipara, white, aged 32 years. Classical cesarean section for placenta previa in eighth month, complicated by severe bronchial asthma. Infant stillborn, anencephalic monster.

Death on eighth postoperative day. Autopsy: bronchicectasis, bronchopneumonia, mitral stenosis, pericardial and pleural effusion; chronic adhesive pericarditis.

8. Multipara, white, aged 39 years. Pregnancy at term. Weight 200 pounds. Entered hospital with hypertension 184/120 to 200/116), albuminuria, glycosuria. Fetal heart tones absent. Immediate classical cesarean section under ether anesthesia; cyanosis and fibrillation during operation. Stillborn fetus weighed 10 pounds, 3 ounces. Death on seventh postoperative day ascribed to pulmonary embolus and associated "heart disease, nephritis, and diabetes."

It is evident from a cursory analysis that poor judgment and disregard for indications and contraindications contributed to at least two of the deaths (Cases 3, 4) and that there was questionable justification for cesarean section in two others (Cases 5, 6). It is pertinent to note that six of the eight deaths occurred in hospitals without well-organized obstetric staffs. Assigning the deaths according to the obstetric complication which formed the indication for abdominal delivery, it is evident that toxemia is still the most serious. Among 73 patients sectioned for toxemia, there were three deaths (4.1 per cent). Placenta previa and premature placental separation were associated with two deaths in 164 cases treated by section, although it is evident that in one of these cases (Case 7) cardiac and pulmonary disease were responsible for the fatal outcome. Infection was the final cause of death in two of eight fatalities. No deaths occurred in 166 elective sections performed because of previous section, in 384 ascribed to cephalopelvic disproportion, or in the 46 following dystocia of various types, exclusive of that associated with malpresentation.

Accurate information is not available concerning the causes of fetal deaths, nor of the maternal states responsible for the cesarean sections followed by fetal losses. Of the 78 infant deaths, 28 (35.8 per cent) are known to have been stillborn, and 25 (32.0 per cent) died neonatally. Thirteen (16.6 per cent) were premature. No data are available concerning twelve. Of the stillbirths, three were nonviable monstrosities. Five fetal deaths were attributed to erythroblastosis.

Discussion

This comparative analysis of cesarean section statistics for the City of Detroit during a span of twenty years shows a noteworthy improvement in maternal mortality, as well as a striking change in thought and practice. The steady rise in hospital confinements to a point where, in 1945, less than 6 per cent of obstetric patients were delivered at home indicates an important change in attitude on the part of the public concerning the importance of hospital facilities for childbearing. The fact, moreover, that 75 per cent of deliveries occurred in the larger and, for the most part, better organized maternity services further attests to the better judgment of the majority of patients in seeking good obstetric facilities. This is borne out by the fact that the over-all maternal mortality of these services (1.1 per 1,000 live births) was lower than that of the city as a whole, and only one-third as great as that of the small hospitals which cared for 19.1 per cent of the total births for 1945. As was stated above, 9 of the 25 smaller hospitals conformed to the standards of the American College of Surgeons. Only 13.3 per cent of the total births for the city, or 14 per cent of hospital births occurred in substandard institutions. The mortality rate for home delivery also exceeded that of the larger maternity services.

Incidence.—A survey of the incidence of cesarean section during the twenty years covered in the study shows that this has increased to a point where abdominal delivery is now practically six times more frequent than in 1925, and four times more than in 1930. In the larger hospitals of the 1945 series (com-

prising 75 per cent of all deliveries and 83.2 per cent of all cesarean sections performed), the incidence ranged from 1.2 to a high of 7.4 per cent, the average being 3.0 per cent. In a recent compilation of cesarean section statistics from the literature, Reis and DeCosta[3] estimated an average incidence of 3.42 per cent, a figure somewhat higher than the over-all incidence for Detroit of 2.77 per cent in 1945. Reis and De Costa's series includes the results of highly specialized clinics as well as those derived from city and state surveys. Probably a better concept of the over-all picture can be obtained by comparing only community statistics. We have, accordingly, compiled published reports from other cities and states and have arranged them in two groups representing earlier and more recent reports, since it is evident that increasing incidence and lowered mortality are now the universal trend. These statistics are summarized in Tables VIII and IX.

As shown in Tables VIII and IX, the average annual incidence in five separate communities from 1921 to 1936, inclusive, was 1.56 per cent, whereas, from 1937 to 1945, this had increased to 2.84 per cent, a figure which is practically identical with that for Detroit in 1945. The highest incidence of 4.07 per cent in Oakland (and in Los Angeles, as shown in Lazard's report cited by Reis and

TABLE VIII. CESAREAN SECTION INCIDENCE AND MORTALITY DURING YEARS 1921-1936

AUTHOR	LOCALITY	YEARS	TOTAL BIRTHS	NO. CESAREAN SECTIONS	INCIDENCE PER-CENTAGE	CESAREAN SECTION DEATHS	MORTALITY PER-CENTAGE
Keettel[4]	Wisconsin	1934	52,932	868	1.64	28	3.23
		1935	53,794	925	1.73	36	3.89
		1936	53,891	1,022	1.90	33	3.23
King[5]	New Orleans	1921-26	61,966	300	0.48	47	16.1
		1927-36	92,936	1,108	1.19	64	5.9
Williams[6]	Philadelphia	1931	33,773	601	1.8	38	6.1
		1932	32,093	591	1.8	36	6.0
		1933	29,228	583	1.7	23	3.9
		1934	29,751	638	2.1	21	3.1
		1935	29,988	703	2.3	32	4.6
		1936	29,652	799	2.7	28	3.6
Welz[1]	Detroit	1925	33,480	154	0.46	20	13.0
Seeley [2]	Detroit	1930	34,007	203	0.59	9	4.43
	Average				1.56		5.92

TABLE IX. CESAREAN SECTION INCIDENCE AND MORTALITY DURING YEARS 1937-1945

AUTHOR	LOCALITY	YEARS	TOTAL BIRTHS	NO. CESAREAN SECTIONS	INCIDENCE PER-CENTAGE	CESAREAN SECTION DEATHS	MORTALITY PER-CENTAGE
Keettel[4]	Wisconsin	1937	55,022	1,021	1.85	35	3.43
		1938	56,213	1,233	2.19	19	1.54
		1939	55,315	1,221	2.21	27	2.21
		1940	56,110	1,439	2.56	32	2.22
Williams[6]	Philadelphia	1937	30,059	811	2.7	20	2.5
		1938	30,739	795	2.6	13	1.6
		1939	30,232	857	2.8	11	1.3
De Normandie[7]	Massachusetts	1937	63,988	2,082	3.2	66	3.1
		1938	64,112	2,216	3.4	60	2.7
		1939	64,340	1,984	3.1	54	2.7
		1940	68,261	2,312	3.4	41	1.7
		1941	63,266	2,436	3.3	52	2.1
Lee[8]	Portland, Ore.	1942	8,547	223	2.60	1	0.45
Bell[9]	Oakland	1943	7,147	290	4.07	2	0.68
--------	Detroit	1945	36,100	1,000	2.7	8	0.80
	Average				2.84		1.93

DeCosta) indicates a much more radical trend in California than in other widely dispersed centers quoted in the literature. The decline in maternal mortality from an average of 5.92 per cent in 1921-1936 to 1.93 per cent in the more recent reports reflects the general trend. The Detroit figure of 0.8 per cent is surpassed only by the smaller series from Portland and Oakland with 0.45 and 0.68 per cent, respectively.

Indications.—With the concomitant increased incidence of cesarean section on the one hand and the lowered mortality on the other, one might well ask whether too many sections are now being performed or whether too few took place in former years. To some extent, both questions can be answered in the affirmative. According to the findings of the Detroit Committee on Maternal Mortality,[11] at least 20 of the 58 maternal deaths of 1945 were considered preventable, and many of these might have been avoided by resort to cesarean section. At the same time, the indications for cesarean section were certainly questionable in several of the eight fatal cases in 1945, as cited above. Granted that cesarean section in competent hands and under ideal circumstances has a low surgical mortality, it nevertheless has a comparatively high obstetric risk. Consequently, it is still difficult to justify extremely high cesarean section rates for the usual cross section of private obstetric patients. Ill-defined indications (notably "disproportion" without pelvimetry or adequate trial of labor) suggest an easy escape from potential difficulties for the obstetrician but with serious possibilities for the patient from the immediate surgical hazards and, in future pregnancies, from the dangers of ruptured uterine scar, repeat section, etc.

According to Seeley's report, the primary factor leading to the lowering of the maternal mortality in Detroit from 1925 (Welz) to 1930 was decreased resort to cesarean section in eclampsia. Despite this lesson, there were eighteen sections for eclampsia in 1945, but with no deaths. In 55 other instances where sections were done in the presence of nonconvulsive toxemia there were three deaths. Two of these (Cases 1 and 2) seem to have been treated adequately (one too long, perhaps) by medical means without benefit, and the outcome could be considered as probably unavoidable, unless one should take the extreme view of opposing cesarean section under any circumstance in toxemia. The third patient (Case 8) was subjected to immediate section in the presence of fetal death without any attempt at first improving her serious condition by treatment. However, she survived the operation to die on the seventh day, allegedly of pulmonary embolism.

Disregard of contraindications and overstepping the bounds of prudence were well illustrated, however, in the case of classical section (rather than cesarean-hysterectomy, or better yet, extraperitoneal section or vaginal delivery) in the presence of evident infection after prolonged labor and ruptured membranes associated with an unrecognized face presentation (Case 3). It is noteworthy that cesarean-hysterectomy (28 cases) and extraperitoneal section (12 cases) resulted in no fatalities, presumably under somewhat similar circumstances. Of the two deaths in 164 instances of hemorrhage, one (Case 4) can be criticized on the grounds of sheer neglect for failure to replace blood loss adequately in a patient approaching exitus. The other (Case 7) died as a consequence of pulmonary and cardiac complications and must be considered nonpreventable. In two other cases, full information was unobtainable. However, in one (Case 6) it is safe to say that death resulted from infection with little justification for the intervention. Complete details of the other (Case 5) are also lacking, but there is information enough to question seriously the employment of classical cesarean section after thirty-six hours of exhausting

labor. Thus, in four of eight deaths, there are reasons to believe that better judgment and more competent management might have prevented the fatal outcome (or the cesarean section) altogether. In spite of the general improvement in cesarean section mortality, it would appear, then, that with respect to the deaths which did occur the situation has not improved since 1930 when Seeley considered that three of nine cesarean section deaths of his series might have been avoided by better regard for indications and contraindications. One wonders how many more errors were masked by antibiotics, chemotherapy, and the blood bank. Our information did not permit clarification of these points by a thorough study of morbidity, which, as Montgomery stated, is the "Mother of Mortality." However, the analysis of the eight maternal deaths in 1945 quite clearly demonstrates that further substantial improvement in results could have been obtained had indications and contraindications been better observed.

Fetal Results.—It is regrettable that more detailed information concerning the fetal deaths was not available. Although the gross infant mortality in 1945 showed a marked decline over the preceding periods, the fact remains (as pointed out by Acken[10] and others) that the fetal mortality rate in cesarean section is definitely higher as a whole than for vaginal delivery. The death rate in Detroit during 1945 for all infants under one year of age was 33.6 per thousand live births, whereas 78 infants were lost at birth or neonatally among the 1,000 cesarean sections—more than twice the city rate for the first year of life. The fact that 36 per cent were known to have been stillborn is further reason for questioning the belief that cesarean section offers the best chances for the child. Granting the possibilities in the argument of those favoring cesarean section that the operation is often done for serious conditions which threaten the life of the child as well as the mother (and also well before term) it is evident that the actual effect of abdominal delivery on the fetal welfare can be determined only by careful study of many cesarean sections from the standpoint of the child, as contrasted to results in vaginal delivery under comparable circumstances. Even should such an analysis show fetal advantage in abdominal delivery, there remain certain features unfavorable to the child in cesarean section which offer a major challenge. Acken and others have discussed the problem of anesthesia, anoxia due to blood loss, and some other factors.

Summary

In Detroit, during 1945, there were 1,000 cesarean sections, or one in 37 births, as contrasted to 154 or one in 217 deliveries in 1925 (Welz), and 203 or one in 167 in 1930 (Seeley). On the other hand, maternal mortality with cesarean section for these series were 13 per cent in 1925, 4.4 per cent in 1930, and only 0.8 per cent in 1945. The fetal death rates for the same years were 11, 12.8, and 7.8 per cent. The incidence of the operation during 1945 in the fourteen larger hospitals with 1,000 or more deliveries varied from one in 78 to one in 13 births, and, in most instances, the 1945 rates represented increases over those for 1925 and 1930, thus reflecting the general trend for the city as a whole. The low cervical operation had become the one most frequently employed by 1945 and, as before, showed distinct maternal advantage over the classical type. Cesarean-hysterectomy and extraperitoneal section were only forty in number but without mortality.

The hospitals were divided into three groups according to numbers of deliveries as follows: 2,000 or more—5 hospitals; 1,000 to 1,999—9 hospitals; and

less than 1,000—25 hospitals. In the first two groups there were 13,997 and 13,130 deliveries with a maternal mortality rate of 1.1 per 1,000 for both. In these same two groups, cesarean sections had incidences of 3.6 and 2.5 per cent, with death rates of 0.39 and 0.62 per cent, respectively. In the third group, there were 6,946 deliveries in the 25 hospitals, with a general maternal mortality of 3.46 per 1,000, and a cesarean section incidence of 2.4 per cent with 2.38 per cent deaths. Moreover, three of the four cesarean fatalities ascribable in whole or in part to questionable treatment occurred in these hospitals.

The number of cesarean sections done for the various indications increased markedly in all important categories. However, the proportional variations remained remarkably constant except for the toxemias of pregnancy. Cesarean sections for these conditions had increased from 26 in 1925 to 73 in 1945, but these figures represented a decrease from 17 per cent of all sections in 1925 down to 7 per cent in 1945. The proportional and absolute increase under the heading "Miscellaneous" is explained in part by some new indications such as "Rh negative."

An outstanding feature, on comparing the three periods, is the marked reduction in cesarean section mortality—from the appalling rate of 13 per cent in 1925, to 4.4 in 1930, and down to only 8 cases or 0.8 per cent in 1945. In spite of this good record for 1945, there was, however, good reason to believe, on the basis of the available data, that poor judgment and disregard of indications and contraindications were largely responsible for two of the eight deaths. In at least two others, the indications for abdominal delivery were highly questionable. Regarding the conditions for which cesarean section was done, the toxemias remain the most serious—three deaths in 73 during 1945. There were also two fatalities among the 164 operations for placenta previa and premature separation of the placenta. No deaths occurred in 166 elective sections performed because of previous cesarean, and none in the 384 done for cephalopelvic disproportion.

Only a few details were secured regarding the fetal deaths. Of the 78 infants lost, 28 (35.8 per cent) are known to have been stillborn, and 25 (32 per cent) were neonatal deaths. At least 13, or 16.6 per cent, were premature infants. Three were maldeveloped, and five deaths were attributed to erythroblastosis.

This analysis of cesarean sections from Detroit led to some interesting conclusions, comparisons with other communities, and other data as follows: A rise in hospital confinements during the twenty years to more than 94 per cent of the deliveries in 1945 was accompanied by a reduction in the general maternal mortality to 1.6 per 1,000 live births. At the same time, there was an increase in cesarean sections from 154 in 1925 to 1,000 in 1945, a percentage of 2.7, or one in 37 births. This high incidence is in accord with the average (2.84 per cent) obtained from the recent studies in various states and cities. The Detroit cesarean section mortality rate of 0.8 per cent compared very favorably with that of these other communities. In Detroit's largest and, generally speaking, better organized obstetric services, there were 75 per cent of the city's deliveries

with a substantially lower over-all mortality. In these hospitals there was also a definitely higher incidence of cesarean section, but again a very low death rate (0.48 per cent). In view of the markedly increased incidence of cesarean sections on the one hand and the greatly decreased mortality on the other, it is well to ask if too many are now being done or if too few were done before. There is evidence that, in 1945, many sections were done for scant reason, to say the least. Apparently there is widespread disregard of the fact that, though the death rate is low, surgically speaking, it represents a high immediate obstetric risk, as well as a definite hazard for future pregnancies. On the other side of the question, it is noteworthy that in 1945 at least 20 of the 58 maternal deaths were considered to have been preventable, a number of them by timely cesarean section. Both sides of the question, then, seem to involve a proper regard for established indications and contraindications. Specifically pointing the way to further improvement, as mentioned before, is the fact that, in at least four of the eight cesarean deaths in 1945, the fatal outcome was in considerable part due to faulty judgment or management.

The fetal mortality rate of 7.8 per cent in the 1945 cesarean sections, though definitely better than in previous years, is still twice the over-all death rate for infants during the first year of life. The fact that 36 per cent were stillborn again emphasizes the fact that cesarean section does not necessarily offer the best chances for a living child. Hence, there is no justification for undue extension of the use of cesarean section for purely fetal indications.

References

1. Welz, Walter, E.: Am. J. Obst. & Gynec. **13**: 361, 1927.
2. Seeley, Ward F.: Am. J. Obst. & Gynec. **24**: 69, 1932.
3. Reis, Ralph and De Costa, Edwin J.: J. A. M. A. **134**: 775, 1947.
4. Keettel, William C.: Wisconsin M. J. **41**: 302, 1942.
5. King, Edward L.: Am. J. Obst. & Gynec. **40**: 860, 1940.
6. Williams, Philip F.: Am. J. Obst. & Gynec. **40**: 866, 1940.
7. De Normandie, Robert L.: New England J. Med. **227**: 533, 1942.
8. Lee, G. P.: West. J. Surg. **53**: 330, 1943.
9. Bell, T. Floyd: West. J. Surg. **53**: 139, 1945.
10. Acken, Henry S.: Am. J. Obst. & Gynec. **53**: 927, 1947.
11. Unpublished data.

Discussion

DR. EDWIN J. DeCOSTA, Chicago.—Detroit is to be congratulated for its exceedingly low maternal death rate and low cesarean section death rate.

For the sake of the record, it seems desirable at this time to compare briefly the Detroit figures with those of Chicago. During 1945, Chicago hospital deliveries, which constitute some 95 per cent of the total deliveries, numbered 59,343, of which 2,177 were cesarean section, a rate of 3.67 per cent. The maternal death rate for the entire group was 1.62 per thousand, for cesarean section 6.4. During the same period, out of the total of 125,016 deliveries in the state of Illinois, the cesarean section incidence was 3.6 per cent.

Dr. Siddall has surveyed 690,000 deliveries in various communities and has concluded that the average community incidence of cesarean section is 2.84 per cent. In a recent publication with Dr. Reis, we estimated this over-all incidence to be 3.42 per cent. According to the state of Illinois, we have been a bit conservative; according to Detroit, a bit radical. It is interesting to note that out of some 45,800 deliveries mentioned by Drs. Tollefson and Krahulik in their discussion of our paper, the incidence of cesarean section in Los Angeles private hospitals was 9.2 per cent, while in Los Angeles County Hospital

it was 3.32 per cent. I mention these variations only to point out that one can reach almost any conclusion depending upon the number of cases reviewed and the area from which the material is gathered.

We all appreciate that the risk of cesarean section is many times greater than the risk of vaginal delivery. Yet hundreds of consecutive cases of cesarean section have been performed in our larger hospitals without a single death. In our own series, this numbered 822 through 1946. But we must not convey to the public the thought that women may be delivered as safely abdominally as vaginally. The records of Detroit and Chicago prove otherwise, and these are most enviable records.

Drs. Mack and Siddall have not stated the source of their figures. I assume that they were provided by the Detroit Department of Health. Unless one has worked with statistics, it is difficult to appreciate the tremendous problems involved in gathering accurate figures concerning the maternal death rate. In a country like ours, where every move from cradle to grave is free and unrecorded, accurate information can be obtained only with great pains.

Comparative studies, such as we have just had the privilege of hearing, are most important in the evaluation of progress and in restraining unbridled surgery. By this method we learn whether or not our efforts are worth while.

DR. GEORGE KAMPERMAN, Detroit, Mich.—In noting the change and improvement in the maternal mortality statistics, it is interesting to consider the factors contributing to this improvement. In the first series reported, we are considering the period when most of the cesarean sections were performed by the general surgeon. It took a long time for obstetrics to gain recognition as a specialty. And the family practitioner, who at first felt the obstetrician was an intruder, much preferred to call on a general surgeon for his sections. The general surgeon was not a true consultant in those instances but was merely a technician who performed the operation on the say-so of the family practitioner. No matter how skillfully the operator had performed, the results were bad, not so much perhaps due to the indications but more because of the contraindications, which were ignored or not considered. From the standpoint of maternal mortality, contraindications are more important even than indications. And the family practitioner in many cases was not cognizant of the fact that he himself was establishing the contraindications. He had not then learned that a first stage of labor can be so conducted that contraindications are practically nonexistent, in case a cesarean section were eventually found indicated. I believe it is the consciousness of contraindications that has been the largest factor in the reduction of maternal mortality. We have learned when *not* to perform a cesarean section.

Another factor has been the recognition that a patient in the acute eclamptic convulsive state is a poor risk for major operations. It also clouded the statistics in that, doubtless, many deaths due to eclampsia were attributed to cesarean section. The conservative treatment of eclampsia has been a factor in reducing the death list from cesarean section.

It will be noted that the incidence of cesarean section shows an increasing frequency. This, no doubt, is due, to a great extent, to the widening of the indications. Obstetrics has become more and more a surgical specialty. Well-trained obstetricians have at their command surgical procedures not possessed by the family practitioner. He, by training, can do certain things for his patient, and he argues that if he can do certain things safely for his patient, why should not his patient have the benefit of his training. As a result, no doubt, many cases are sectioned simply because the labor promises to be very difficult.

This means that obstetric practice is coming to a new cross road. Cesarean section is now becoming so safe an operation that the obstetrician, often on the insistence of the patient, is induced to perform a section rather than let the patient have a normal, although difficult, delivery.

I am glad the essayist calls attention to the fact that although cesarean section is becoming a safer operation, vaginal delivery, in the majority of cases, is still the safer procedure. Obstetricians should stop, look, and listen, to make sure that cesarean section, so valuable a procedure, is indicated and is not abused so that it may become a menace to our patients.

DR. E. L. KING, New Orleans, La.—We conducted a study in 1926 for the previous six years and again in 1930 for a ten-year period. From 1921 to 1926 there were a little over 61,000 births in our city. One-fourth of these were delivered in hospitals. There were 300 cesarean sections performed, a ratio of 1:206. In the second series, there were 92,900 deliveries with about 60 per cent delivered in hospitals, 1,108 cesarean sections were performed, or a ratio of 1:84. During the past five years, 74,810 deliveries have occurred in New Orleans, approximately 71,000 being delivered in hospitals, or 96 per cent hospital deliveries in the past five years, with 2,720 cesarean sections, a ratio of 1:28.

In the first series, there was 15 per cent maternal mortality. In the second series, 64 of the 1,108 cesarean section patients died, a percentage of 5.9. Of the 2,720 cesarean sections in the last five-year period, there were thirty-three deaths, or 1.21 per cent.

In the first series, there was a fetal mortality rate of 18 per cent, but it should be remembered that this includes statistics from Charity Hospital where there were many complicated cases.

DR. RUDOLPH HOLMES, Charlottesville, Va.—I had the misfortune of beginning practice when there was only one indication for section and that was gross disproportion.

I think craniotomy still has its place in obstetrics. Within the range of indications for it, craniotomy is the safest operation a parturient may have, and it is the wise procedure to follow when the infant is a monster, living or dead. I think that cesarean section is being done too often. The smaller the hospital, the higher the incidence of cesarean section and the higher the incidence of death. In Illinois the highest incidence of cesarean section was in the smallest country hospitals. That is not right.

DR. MACK (Closing).—It is very gratifying to learn of the downward trend in cesarean section mortality in other communities, as has been brought out in the discussion. One purpose of this study was to show that community figures give a better over-all picture of the operation than is derived from statistics of individual hospitals or clinics. The public gains a false sense of security from hospital reports with high incidence and low mortality. As Dr. King pointed out, bad results are still obtained, to a large extent in substandard hospitals, where the indications and contraindications are not properly heeded. We believe that even with modern facilities no one should dare to take undue liberty with indications or contraindications.

SERUM BETA-GLUCURONIDASE LEVELS DURING TOXEMIA OF PREGNANCY*

LESTER D. ODELL, M.D., AND DONALD F. MCDONALD, M.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology and Department of Surgery, The University of Chicago and The Chicago Lying-in Hospital)

FOR some time science has sought a specific chemical or biologic fraction or reaction, the presence, absence, or concentration of which would identify the toxemias of pregnancy. To be ideal, such a test should probably possess several characteristics; it should be specific for that syndrome, it should warn the obstetrician of an impending toxemia, it should distinguish pre-eclampsia from essential hypertension, it should be of prognostic value, and the method of analysis should be relatively easy and accurate. In general, attempts in this direction have been along chemical, biologic, hormonal, or enzymatic lines. In regard to the first three of these, studies have been largely concerned with the blood uric acid level,[1] the uric acid clearance,[2-4] reaction to pituitrin[5] and cold pressor tests,[6] serum estrogen[7, 8] and gonadotropin levels,[9] and urinary pregnandiol excretion.[10, 11]

Pregnancy and toxemia of pregnancy cause many metabolic changes which may be manifested in alterations of the enzyme structure of the organism.

Abderhalden[12] noted that serum from pregnant women, incubated with placental tissue in a dialyzing tube, liberated amino acids which could be identified in the dialysate. This reaction became the basis for a pregnancy test. Dieckmann[13] found the Abderhalden negative in some eclamptic patients. Obata[14] found normal and eclamptic blood serum and placental extract lethal for white mice in equivalents; serum from normally pregnant patients, however, incubated with placental extract, inactivated placental toxin, whereas eclamptic serum did not. Obata believed the reaction an antigen-antibody one. Hayashi[15] discovered that the detoxification effect was destroyed at room temperature in four to five days, or upon heating to 50 to 60 degrees for one-half hour, thereby suggesting its enzymatic nature. Dieckmann,[16] using mice, confirmed Obata's results and devised a different method based on the clotting mechanism (employing the technique of Loeb and co-workers[17]) for testing the neutralizing substances. Clotting of the plasma was delayed if serum was obtained from eclamptic patients. Dieckmann concluded that there was no specific placental toxin since extracts of beef lung gave the same response. Recently, Schneider[18, 19] has revived these experiments and has identified the placental toxin as thromboplastin.[20]

Von Fekete,[21] using a bioassay employing guinea pig intestine strip, found pregnancy serum would inactivate the oxytocic factor in solution posterior pituitary, the basis of Page's[22] pitocinase test for pregnancy. Aragon[23] tested

*Read before the Central Association of Obstetricians and Gynecologists, Oct. 25, 1947, Louisville, Ky.

serum from normally pregnant and toxemic patients, using Page's method, and found a progressive increase in pitocinase during normal pregnancy. Values for toxemic patients, however, were scattered on either side of the normal curve and consequently were of no diagnostic or prognostic value.

Smith and Smith[24] reported an increased fibrinolytic activity of the blood serum during pre-eclampsia, less in hypertensive patients with superimposed pregnancy. Willson and Munnell,[25] however, were unable to use it for accurately differentiating between "vascular renal disease and the specific pregnancy toxemias." Moreover, fibrinolysis tended to be increased in those patients exhibiting proteinuria irrespective of the type of toxemia studied. And fibrinolysins are found in many nonpregnant conditions.

Among other reports are these: Histaminase[26] (bio-assay) increases five hundredfold to a thousandfold during pregnancy and may be employed as a prognostic guide in abortions. Contradictory reports exist concerning this enzyme during toxemia of pregnancy, it being lowered according to some[27, 28] and normal according to another.[29] Renin[30] is increased during eclampsia. Plasma lipase[31] falls during pregnancy, whereas blood amylase[32] is more active. Angiotonase[33] increases four- to tenfold during the second half of normal pregnancy, but values from toxemic patients are not significantly altered. Serum cholinesterase[34] is lower during normal pregnancy.

We[35] have previously reported on the serum beta-glucuronidase activity during normal and toxemic pregnancy and upon certain organ tissues. We found the mean curve during normal pregnancy to increase from 3 μg at three months to 13.5 near term. Values during pre-eclampsia were higher, usually above 20, whereas those for hypertensive toxemia were within the normal range. We postulated that beta-glucuronidase levels might be employed to differentiate pre-eclampsia from hypertensive toxemia of pregnancy. An analysis of various tissues failed to suggest the site of formation of the enzyme.

The purposes of this report are (1) to re-emphasize the differentiation by serum beta-glucuronidase values of pre-eclampsia and hypertensive toxemia of pregnancy; (2) to illustrate the use of beta-glucuronidase levels in detecting a potential pre-eclampsia; (3) to point out that beta-glucuronidase values are apparently of no prognostic value; (4) to report levels for convulsive toxemia of pregnancy; (5) to illustrate examples of toxemia of pregnancy in which repeated serum levels of enzyme were obtained and to correlate these with the clinical course of the disease.

Materials and Method

A total of 118 patients were studied. These consisted of seventy-nine with toxemia of pregnancy and forty-five with excessive weight gain. Some of the latter developed a toxemia. In addition, there was one patient with a functional amenorrhea and superimposed pregnancy and another with uremia.

The method of analysis was that described by Tallalay, Fishman, and Huggins.[36]

Basis of Diagnosis.—According to established recommendations, the toxemias of pregnancy may be classified as follows: (1) conditions peculiar to pregnancy such as (a) pre-eclampsia and (b) eclampsia and coma; (2) conditions not peculiar to pregnancy, including essential hypertension, malignant hypertension, acute and chronic nephritis, and pyelonephritis. In this study

we have considered nonconvulsive patients as being either pre-eclamptic or hypertensive, since no known cases of nephritis, malignant hypertension, or pyelonephritis were observed. In addition, we have grouped cases of recurrent toxemia with the hypertensive patients.

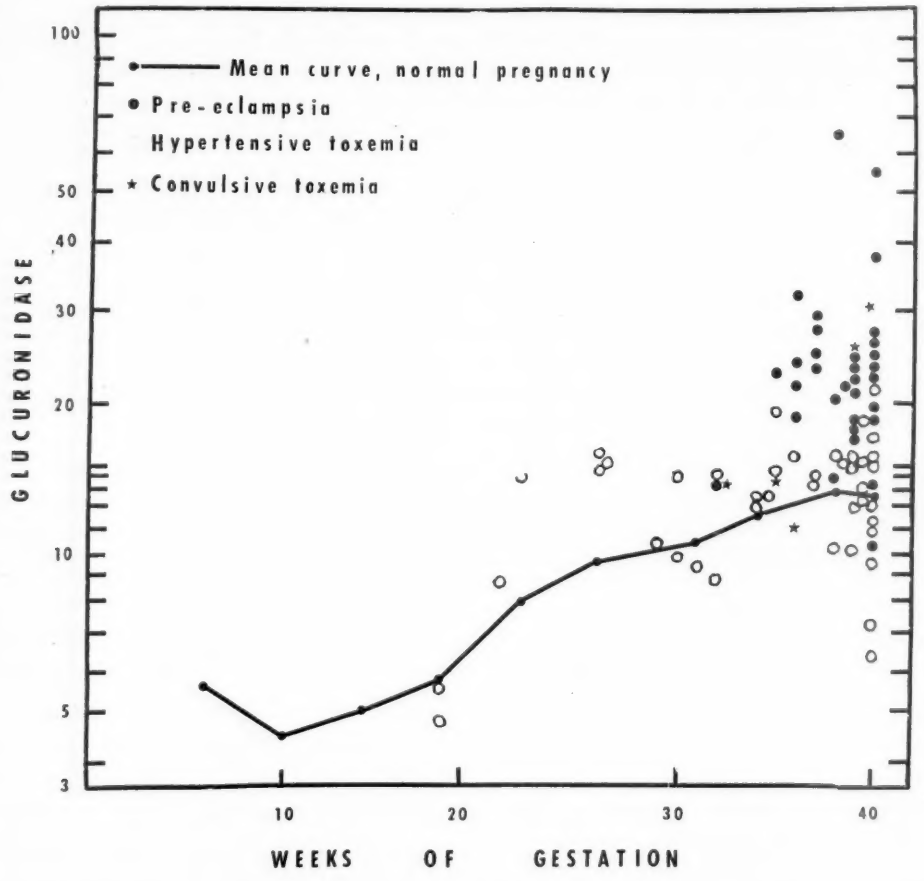


Fig. 1.—Serum glucuronidase. Toxemia of pregnancy (semi-log scale).

Certain clinical characteristics have become associated with pre-eclampsia and hypertensive toxemia, among which may be mentioned the following: Age distribution is higher in hypertensive toxemia than in pre-eclampsia. Multigravidity is more characteristic of hypertensive patients. Too rapid weight gain (edema) is mostly found during pre-eclampsia. Averages for systolic and diastolic blood pressure are lower during severe pre-eclampsia than during severe hypertensive toxemia. The onset of toxemia is earlier in the latter group and its duration more prolonged post partum. And hypertensive patients more often possess a family background for vascular disease. The data in Table I compare favorably with that reported by Dieckmann.[13]

Using these criteria, thirty-three patients were judged to have pre-eclampsia; five, eclampsia*; and forty-two, hypertensive toxemia of pregnancy. Inasmuch as some of those believed to have mild hypertensive toxemia were

*One pre-eclamptic patient under observation subsequently developed eclampsia.

primigravidas, a subsequent follow-up through successive pregnancies will be necessary to establish conclusively that they suffer from early hypertensive vascular disease.

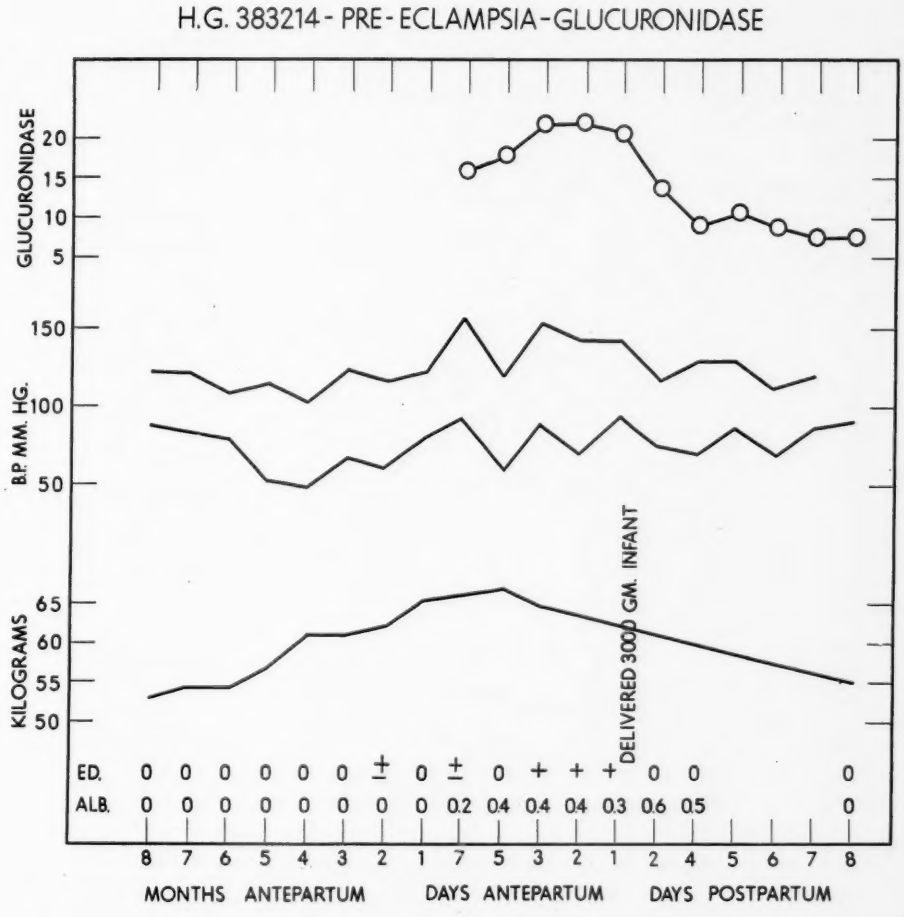


Fig. 2.—H. G. (383214). Age, 23 years, para, 0, gravida, 1; due March 4, 1947; delivered Feb. 13, 1947. Pre-eclampsia. Glucuronidase reported as micrograms per cubic centimeter.

Pre-eclampsia.—Although the upper range for normal pregnancy does not exceed 17.5 μg per cubic centimeter at term,[35] with few exceptions serum beta-glucuronidase values were high during pre-eclampsia. In fact, a figure above 20 μg seemed diagnostic for this condition. Some unusually high values were encountered (Fig. 1). Figs. 2 and 3 are composite graphs for pre-eclamptic patients. Serum beta-glucuronidase levels tended to remain elevated during some of the duration of the disease. Our experience failed to attach much prognostic value to the test after the syndrome appeared. In one pre-eclamptic patient a relatively normal value (13.4 μg) was encountered just previous to delivery, but this patient experienced an eclamptic seizure seventeen hours post partum. In another (Fig. 2) the proteinuria and blood pressure and edema increased steadily without a progressive elevation of the enzyme. In fact, the concentration tended to rise toward a plateau, both before and during the disease, and then in some instances to fall to even normal levels, although the syn-

drome still persisted (Figs. 2 and 3). During the puerperium the concentration fell rapidly, except for slight rises on the fourth to sixth days, possibly due to changes in hormone metabolism or perhaps the result of a mild endometritis.

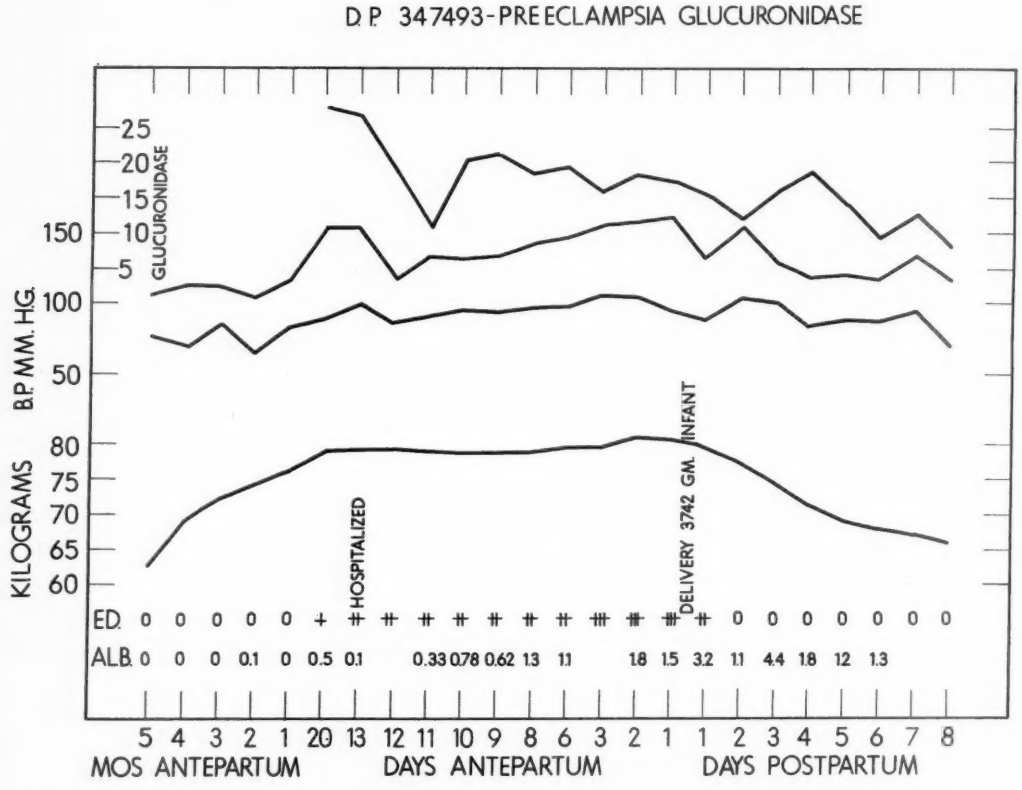

D.P. 347493-PRE ECLAMPSIA GLUCURONIDASE
GLUCURONIDASE
25
20
15
10
5
B.P. MM. HG.
150
100
50
KILOGRAMS
80
75
70
65
60
HOSPITALIZED
DELIVERY 3742 GM. INFANT
ED. 0 0 0 0 0 + + + + + + + + + + + 0 0 0 0 0 0 0
ALB. 0 0 0 0.1 0 0.5 0.1 0.33 0.78 0.62 1.3 1.1 1.8 1.5 3.2 1.1 4.4 1.8 1.2 1.3
5 4 3 2 1 20 13 12 11 10 9 8 6 3 2 1 1 2 3 4 5 6 7 8
MOS ANTEPARTUM
DAYS ANTEPARTUM
DAYS POSTPARTUM

Fig. 3.—O. P. (347493). Age, 30 years, para, 0, gravida, i; due Jan. 30, 1947; delivered Feb. 9, 1947. Pre-eclampsia. Glucuronidase reported as micrograms per cubic centimeter.

Hypertensive Toxemia.—Most levels were within the range for normal pregnancy. Several patients were observed as long as five months without an elevation of serum beta-glucuronidase, one of which is portrayed graphically (Fig. 4). It will be noted that this patient, and the one whose levels are shown in Fig. 5, exhibited considerable proteinuria without an elevation of enzyme concentration in the serum.

Convulsive Toxemia.—Five patients were observed who had convulsions. Case histories are as follows:

CASE 1.—F. S.,* para 0, gravida i, aged 15 years, due July 2, 1947, was first observed on Dec. 16, 1946, with a normal blood pressure and no edema or proteinuria. The subsequent prenatal course was uneventful except for a weight gain of 2 kilograms between April 21 and May 5 and headache on this last visit. On June 1, 1947, labor commenced spontaneously and the patient was delivered spontaneously of a living female infant weighing 3,600 grams. At that time the blood pressure was 140/110, edema 1 plus, and urine negative for protein. Three hours later one convulsion occurred; blood pressure was 144/100 and urine 1 plus pro-

*Patient from another hospital.

teinuria. Subsequently, however, the blood pressure and urine returned rapidly to normal. The puerperium was uncomplicated. The serum beta-glucuronidase level at the time of convulsive seizure was 25.2 μg per cubic centimeter.

CASE 2.—M. G.,* para 0, gravida i, aged 18 years, due Feb. 27, 1947, was first observed on Feb. 4, 1947, with a normal blood pressure, 2 plus edema, and normal urine. On February 12 the patient experienced headache and scotomas, followed by six convulsions. Examination at that time disclosed a blood pressure of 170/120, 2 plus edema, and 2 plus proteinuria. Following premature artificial rupture of the membranes, labor commenced spontaneously and the patient was delivered by low forceps of a living female infant weighing 3,000 grams. Blood pressure and urine returned rapidly to normal during the puerperium. The serum beta-glucuronidase level at the time of convulsive seizures was 30 μg per cubic centimeter and subsequent levels were 27, 25, 32, 20, 19, 19, and 7 μg during the succeeding several days.

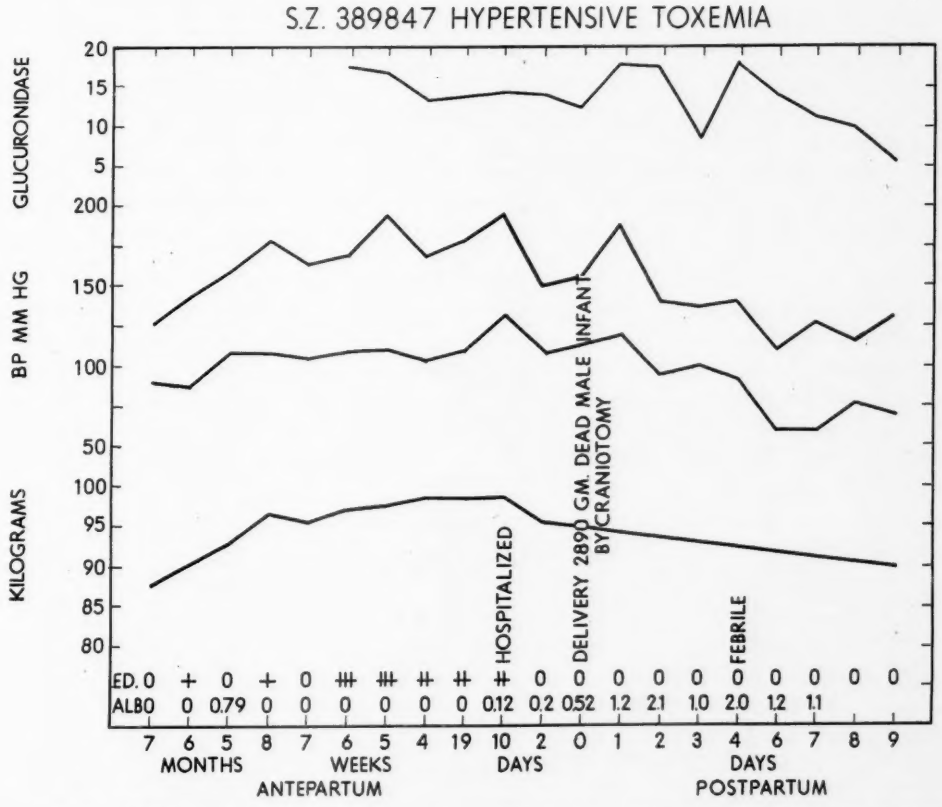

S.Z. 389847 HYPERTENSIVE TOXEMIA
GLUCURONIDASE
BP MM HG
KILOGRAMS
HOSPITALIZED
DELIVERY 2890 GM. DEAD MALE INFANT BY CRANIOTOMY
FEBRILE
ED. 0 + 0 + 0 ++ ++ + + + 0 0 0 0 0 0 0 0 0 0
ALB 0 0 0.79 0 0 0 0 0 0 0.12 0.2 0.52 1.2 2.1 1.0 2.0 1.2 1.1
7 6 5 8 7 6 5 4 19 10 2 0 1 2 3 4 6 7 8 9
MONTHS
WEEKS
DAYS
ANTEPARTUM
DAYS
POSTPARTUM

Fig. 4.—S. Z. (389847). Age, 32 years; para, 0, gravida, 1; due March 22, 1947, delivered March 17, 1947. Hypertensive toxemia. Glucuronidase reported as micrograms per cubic centimeter.

CASE 3.—M. K., No. 403354, para 0, gravida i, aged 19 years, due May 14, 1947, was first observed on March 19, 1947, with headache, blurring of vision, blood pressure 160/114, 3 plus edema, and 4 plus proteinuria. Labor commenced spontaneously on that date and the patient was delivered of a living female infant weighing 1,190 grams by low forceps operation. Seventeen hours later one convulsion occurred, followed by a short period of coma. The subsequent puerperium was uncomplicated. Blood pressure on discharge was

*Patient from another hospital.

140/90 and urine negative for protein. The serum beta-glucuronidase level at the time of delivery was 13.4 μg per cubic centimeter, only slightly above the average for normal pregnancy at the age of gestation. No subsequent levels were obtained.

CASE 4.—J. G.,* para 0, gravida i, aged 17 years, due June 26, 1947, was first observed on May 1, 1947, with a history of a weight gain of seventy-three pounds, headache, dizziness, vomiting, and blurring of vision. Examination disclosed a blood pressure of 210/150, 4 plus edema, and proteinuria. One convulsion occurred on May 2, 1947, followed by two days of coma. The blood pressure, during this period, fluctuated between 240 and 160 systolic and 150 and 102 diastolic. The patient was considered moribund on several occasions. A living female infant weighing 1,700 grams was delivered by cesarean section on May 3, 1947. During the twenty-five days of postpartum hospitalization all edema disappeared, the blood pressure gradually fell to 150/100, but the proteinuria persisted. Serum glucuronidase levels were 11.8 μg per cubic centimeter on May 2, 1947, the day of convulsion, and 5.8, 6.4, 5.8, and 9.8 μg during the succeeding four days. The urea clearance test was 30 per cent of normal at the time of discharge from the hospital.

CASE 5.—M. T., No. 320650, para 2, gravida iii, aged 40 years, due April 15, 1947, was first seen on March 14, 1947, in coma of four hours' duration. Previous to its onset, the patient had complained of severe headache and vomiting. There was a five-year history of hypertension. Examination disclosed blood pressure of 200/110, pulse 120/minute, 4 plus proteinuria, and slight edema. One convulsion occurred three hours after admission. Membranes were ruptured artificially, labor commenced immediately, and the patient was delivered by low forceps of a living female infant weighing 1,855 grams. This case is portrayed graphically in Fig. 5.

It is believed the first three are illustrative of typical eclampsia. Note the rapid onset and rapid disappearance of hypertension, edema, and proteinuria incident to recovery. The fourth patient exhibited blood pressures above 200 mm. systolic, had more persistent hypertension and proteinuria post partum, and had a reduced urea clearance rate on discharge. And the last patient had evidence of residual vascular damage following the experience. It is doubtful if this last case was true eclampsia, being more probably hypertensive encephalopathy.

TABLE I. SUMMARY OF CLINICAL DATA

	PRE-ECLAMPTIC	HYPERTENSIVE	ECLAMPTIC
Total patients	33	42	5
Average age	25	29	25
Per cent primiparas	71	47	80
Per cent > gain of 12 kilograms	66	19	60
Per cent > 180 B.P.	6	30	60
Per cent > 1.5 Gm./24 hr. of protein	50	19	60
Per cent onset < 34 weeks	13	65	60
Per cent family history of hypertension	37	70	20

From these results it is obvious that serum beta-glucuronidase levels are not elevated during all cases of convulsive toxemia of pregnancy.

Abnormal weight gain.—At the Lying-in Hospital patients exhibiting an abnormal weight gain during pregnancy† are followed in the toxemic clinic. The caloric intake in such patients is evaluated by a dietician.‡ If the rapid weight gain persists, particularly after twenty-eight weeks, or if edema appears,

*Patient from another hospital.

†More than an average of 0.6 kilograms per week.

‡The normal prenatal diet consists of: 1,747 calories, 85 Gm. of protein, 181 Gm. of COOH, and 76 Gm. of fat.

a pre-eclamptic diet* is recommended. In this study forty-five such patients were selected at random after twenty-eight weeks of pregnancy and from one to four serum beta-glucuronidase levels obtained every one, two, or three weeks. In none of these had edema, hypertension, or proteinuria as yet appeared. Of this group, thirteen eventually developed two or more of the cardinal signs of toxemia: edema, proteinuria, and hypertension. Of these, six were judged to have pre-eclampsia. Of those who did not develop toxemia, two had had a previous toxemia, presumably a pre-eclampsia. Fig. 6 illustrates the findings. Note the consistently higher values in cases developing pre-eclampsia. One of these (Case 15, Fig. 6) was observed for eight weeks previous to the onset of

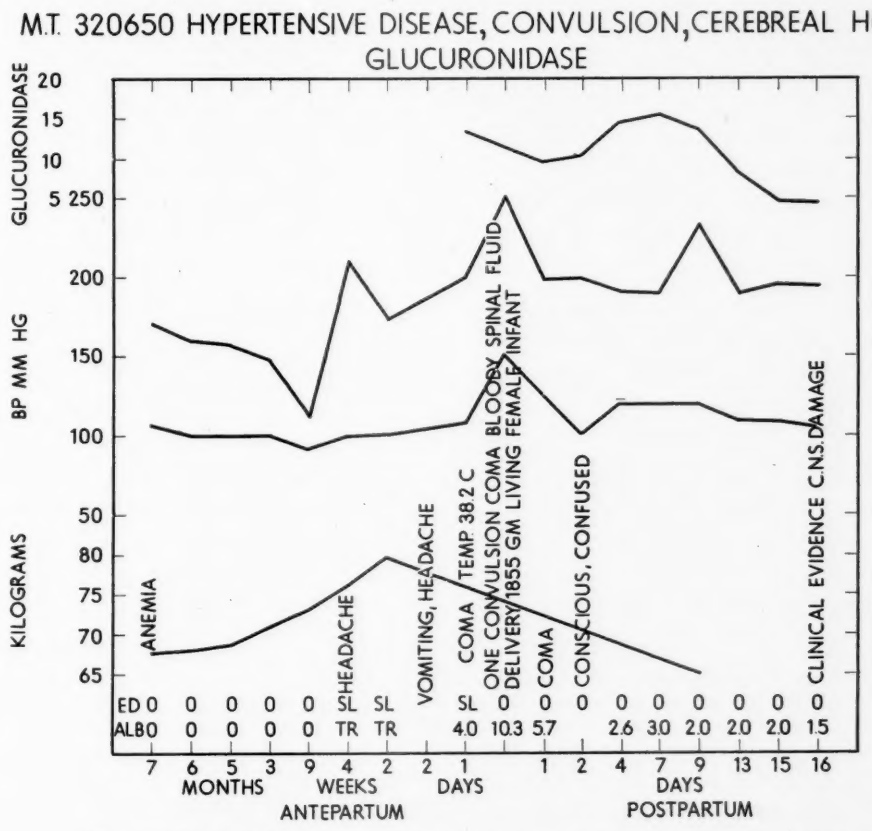

M.T. 320650 HYPERTENSIVE DISEASE, CONVULSION, CEREBREAL HEMORRHAGE.
GLUCURONIDASE
GLUCURONIDASE
BP MM HG
KILOGRAMS
ANEMIA
HEADACHE
VOMITING, HEADACHE
TEMP 38.2 C
COMA
ONE CONVULSION COMA BLOODY SPINAL FLUID
DELIVERY 1855 GM LIVING FEMALE INFANT
COMA
CONSCIOUS, CONFUSED
CLINICAL EVIDENCE C.N.S. DAMAGE
ED 0 0 0 0 0 SL SL SL 0 0 0 0 0 0 0 0 0
ALB 0 0 0 0 0 TR TR 4.0 10.3 5.7 2.6 3.0 2.0 2.0 2.0 1.5
7 6 5 3 9 4 2 2 1 1 2 4 7 9 13 15 16
MONTHS WEEKS DAYS DAYS
ANTEPARTUM POSTPARTUM

Fig. 5.—M. T. (320650). Age, 40 years, para, 2, gravida. iii; due April 15, 1947; delivered March 14, 1947. Hypertensive disease, convulsion, and cerebral hemorrhage. Glucuronidase reported as micrograms per cubic centimeter.

the syndrome. Note also that most values are in excess of the mean curve for normal pregnancy, suggesting that beta-glucuronidase levels are closely allied to water retention. Inasmuch as these patients were treated for potential pre-eclampsia, and received dietary advice, it is reasonable to suppose that their medical and obstetric management may have averted other cases. Of those patients who developed a toxemia but did not have pre-eclampsia, two had recurrent toxemia. The remainder (five patients) had a slight hypertension

*The pre-eclamptic diet is the same as the normal diet but contains less than 3.0 Gm. of NaCl per day.

during labor (less than 160 systolic), without a proteinuria and with little edema. According to past experience at this clinic many such cases represent early manifestations of hypertensive vascular disease.

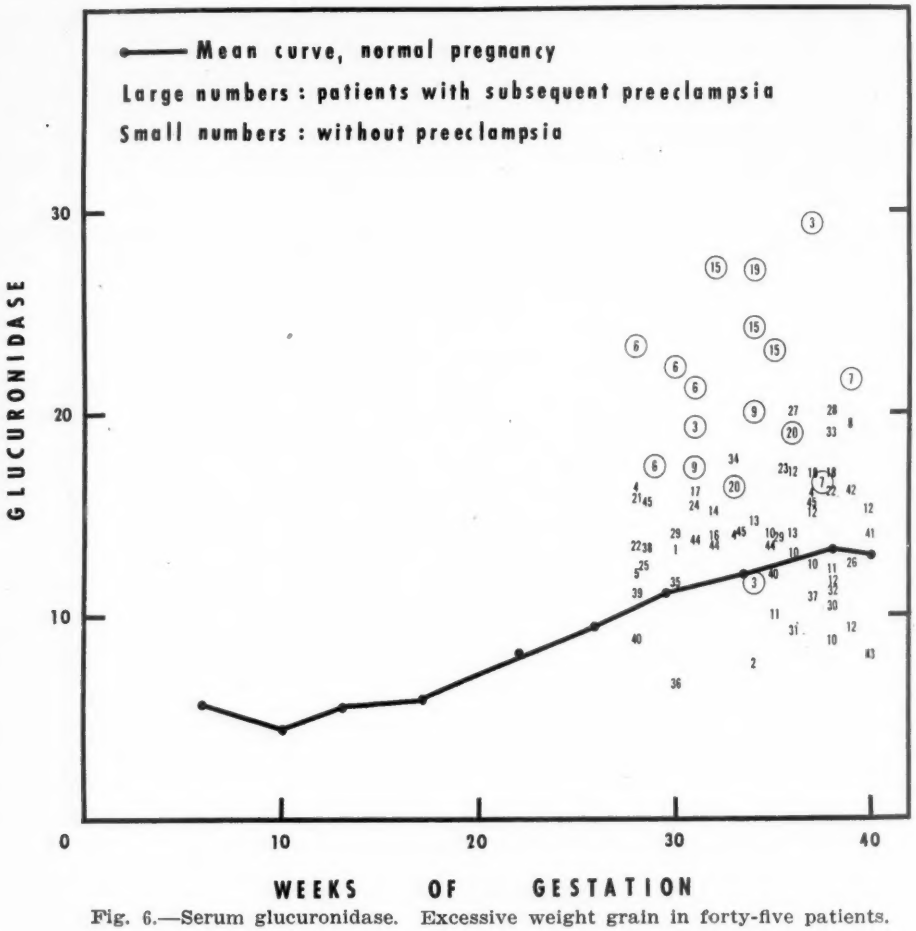


Fig. 6.—Serum glucuronidase. Excessive weight grain in forty-five patients.

Comment

The biologic characteristics of beta-glucuronidase have been studied by Fishman[37-40] and by Fishman and Fishman.[41] Fishman found an increase of enzyme activity in the vital organs (liver, spleen, and kidney) of animals fed nonestrogenic glucuroniogenic substances, whereas ovariectomized mice on estrogens show a 100 per cent elevation in uterine beta-glucuronidase without an increase in liver concentration. The enzyme, then, is responsible for the conjugation of estrogens in the uterus.[42] In addition, beta-glucuronidase is concerned with the liberation of pregnandiol since the latter is excreted as a glucuronide ester, and it is involved in the detoxification of hydrocarbon poisons[43] as well as in the metabolism of many other substances.

Although no figures are available for uterine estrogens during preeclampsia, it is known that their placental and serum concentration[9] is low during that disease, as is the urinary excretion of pregnandiol.[10, 11] The high

serum concentration of beta-glucuronidase during pre-eclampsia in the presence of a low serum, urine, and tissue substrate (estrogens and progesterone products) would seem puzzling but may be explained in the metabolism of the latter.

As yet the intermediary metabolism of steroids is incompletely understood. Progesterone, administered parenterally, cannot be entirely accounted for as urinary pregnandiol during pregnancy.[44] So the latter apparently represents only a fraction of the end product of progesterone. The intermediary phases of estrogen metabolism are similarly obscure. If such is the case the serum elevation of beta-glucuronidase during pre-eclampsia merely reflects some unknown disturbance in the metabolism of sex hormones.

In support of this are the following facts: During pregnancy the serum estrogens and urinary pregnandiol (part of the substrate) increase progressively, as does the serum concentration of beta-glucuronidase. Just preceding, or immediately following, the onset of pre-eclampsia there is a sudden rise in serum enzyme concentration, but this gradually declines during a period when hormone levels are reported as decreased.[9-11] In this study only one patient without pre-eclampsia had consistently high levels of enzyme, 56 to 59 μg per cubic centimeter. In this case the last menstrual period occurred in January, 1946, and delivery in May, 1947, an amenorrhea of seventeen months' duration.

The high levels of beta-glucuronidase during pre-eclampsia is probably not due to failure of excretion. One patient with a terminal uremia had a level of 5.6 μg per cubic centimeter, within the range for the nonpregnant individual.[35]

From the results of this study it would seem serum beta-glucuronidase levels could be used to differentiate pre-eclampsia from hypertensive toxemia. But of possible greater importance would be its use to delineate those patients with excessive weight gain who are destined to develop pre-eclampsia from those who are not. Ordinarily prenatal patients visit this clinic every three weeks for the first thirty-four weeks and every two weeks thereafter. The increased frequency of visits during the last trimester is partly because a pre-eclampsia might occur. Serum beta-glucuronidase determinations, obtained at three-week intervals, after twenty-eight weeks' gestation, might warn the obstetrician previous to such an eventuality.

Although the method of preparation of the substrate is difficult, the colorimetric analysis of the enzyme is easy enough for the average laboratory technician. Difficulties with the substrate could be solved by commercial preparations of that substance. It remains stable, as does the serum enzyme. The method of analyses is accurate, being reported within 2 per cent.[36]

Conclusions

1. Serum beta-glucuronidase levels will differentiate most cases of presumable pre-eclampsia and hypertensive toxemia of pregnancy.

2. Glucuronidase levels may warn the obstetrician of an impending pre-eclampsia.

3. The serum concentration of the enzyme does not reflect the severity of the toxemia.

4. Levels during convulsive toxemia are not diagnostic.

5. The serum concentration of beta-glucuronidase apparently reaches a maximum just before, or early in the course of, pre-eclampsia, and then falls during the duration of the syndrome.

References

1. Stander, H. J., and Cadden, J. F.: Am. J. Obst. & Gynec. **28**: 856, 1934.
2. Noyer, A. S. M.: J. Obst. and Gynec. **46**: 722, 1943.
3. Schaffer, N. K., Dill, L. V., and Cadden, J. F.: J. Clin. Investigation **22**: 201, 1943.
4. Bonsnes, R. W., and Stander, H. J.: J. Clin. Investigation **25**: 378, 1946.
5. Dieckmann, W. J., and Michel, H. L.: Am. J. Obst. & Gynec. **33**: 131, 1937.
6. Dieckmann, W. J., and Michel, H. L.: Arch. Int. Med. **55**: 420, 1935.
7. Smith, G. V. S., and Smith, O. W.: Proc. Soc. Exper. Biol. & Med. **30**: 918, 1933.
8. Rakoff, A. E.: Am. J. Obst. & Gynec. **38**: 371, 1939.
9. Smith, G. V. S., and Smith, O. W.: Am. J. Obst. & Gynec. **38**: 618, 1939.
10. Bachmann, C., Lukley, D., and Hirschmann, H.: J. Clin. Endocrinal. **1**: 206, 1941.
11. Browne, J. S. L., Henry, J. S., and Venning, E. H.: J. Clin. Investigation **17**: 503, 1938.
12. Abderhalden, E.: Die abderhaldinsche reakton. Ferment forsch. Leipz. **8**: 245, 1925.
13. Dieckmann, W. J.: The Toxemias of Pregnancy, St. Louis, 1941, The C. V. Mosby Co.
14. Obata, I.: J. Immunol. **4**: 111-139, 1919.
15. Hayashi, T.: Arch. f. Gynäk. **119**: 503, 1923.
16. Dieckmann, W. J.: Proc. Soc. Exper. Biol. & Med. **26**: 239, 1929.
17. Loeb, L., Fliescher, W., and Tuttle, S.: J. Biol. Chem. **51**: 461, 1922.
18. Schneider, C. L.: Am. J. Physiol. **146**: 140, 1946.
19. Schneider, C. L.: Proc. Soc. Exper. Biol. & Med. **62**: 322, 1946.
20. Schneider, C. L.: Am. J. Physiol. **149**: 123, 1947.
21. Von Fekete, K.: Endokrinologie **7**: 364, 1930.
22. Page, E.: Am. J. Obst. & Gynec. **52**: 1014, 1946.
23. Aragon, G. T.: In publication.
24. Smith, O. W., and Smith, G. V. S.: Proc. Soc. Exper. Biol. & Med. **59**: 119, 1945.
25. Willson, J. R., and Munnell, E. R.: Proc. Soc. Exper. Biol. & Med. **62**: 277, 1946.
26. Ahlmark, A.: Lancet **2**: 406, 1944.
27. Werle, E., and Effkemann, G.: Arch. f. Gynäk. **170**: 82, 1940.
28. Kapiller-Adler, R.: Biochem. J. **38**: 270, 1944.
29. Kolozynoki, E. W.: J. Obst. & Gynaec. Brit. Emp. **52**: 486, 1945.
30. Dexter, L., and Haynes, F. W.: Proc. Soc. Exper. Biol. & Med. **55**: 288, 1944.
31. Scoz, G.: Arch. di fisiol. **42**: 109, 1942.
32. Morosi, G.: Arch. di fisiol. **42**: 222, 1942.
33. Page, E.: Am. J. M. Sc. **213**: 715, 1947.
34. Tourtellotte, W., and Odell, L. D.: Unpublished data.
35. McDonald, D. F., and Odell, L. D.: J. Clin. Endocrinol. **7**: 535, 1947.
36. Tallalay, P., Fishman, W. H., and Huggins, C.: J. Biol. Chem. **166**: 757, 1946.
37. Fishman, W. H.: Canad. Chem. and Metallurgy **21**: 410, 1937.
38. Fishman, W. H.: J. Biol. Chem. **123**: xxxvl, 1938.
39. Fishman, W. H.: J. Biol. Chem. **131**: 225, 1939.
40. Fishman, W. H.: J. Biol. Chem. **136**: 229, 1940.
41. Fishman, W. H., and Fishman, L.: J. Biol. Chem. **152**: 487, 1944.
42. Fishman, W. H.: J. Biol. Chem. **169**: 7, 1947.
43. Deickmann, W., and Thomas, G.: J. Indust. Hyg. & Toxicol. **25**: 286, 1943.
44. Davis, M. E., and Fugo, N. W.: Proc. Soc. Exper. Biol. & Med. **65**: 283, 1947.

Discussion

DR. CARL P. HUBER, Indianapolis, Ind.—Anything which serves to differentiate the toxemias of pregnancy into their various groups is certainly worthy of complete investigation. The results reported in this paper seem to give a clue along that line. The authors show very definitely that serum beta-glucuronidase levels are, on the average, above the normal line in the pre-eclamptic group of patients and that in the hypertensive patients they average much lower. It would appear that studies along these lines would be of definite value in differentiating these two groups of pregnant patients and would serve to reinforce our clinical interpretation concerning them. More important perhaps is the observation which is made in the latter part of the paper in which it is shown that among those patients with

excessive weight gain it is possible to pick out the group destined to develop additional evidence of pre-eclampsia by the study of beta-glucuronidase levels. It is quite obvious that we will have to learn a great deal more about the enzymes if we are going to understand many of the complications that arise in pregnancy and that have previously been obscure.

Glucuronidase is one of the enzymes essential in various phases of carbohydrate metabolism and is very probably an important factor in progestin and estrogen metabolism. Its study, therefore, is a step in the investigations that have been made concerning hormone levels during pregnancy and in the toxemias of pregnancy. It is only one step, however, and it does not completely explain the variations that have occurred. Like all catalysts, glucuronidase may act in one of two directions. The mere fact that in the pre-eclamptic toxemia of pregnancy there is a high level of glucuronidase in the serum does not mean that there has been an increased metabolism of the estrogens and progestin. It may mean that there has been a failure of the utilization of the glucuronidase due to some lack of intermittent steps that may be associated with their metabolism. It does not even necessarily mean that there is any connection with hormone metabolism, but these changes may be associated with the metabolism of other toxic products that are produced in pre-eclamptic patients. A great deal more work obviously must be done before we have a complete understanding of the situation.

Dr. Odell did not give any description of the complicated procedures associated with the test, and from the practical standpoint for those who do not have the same laboratory facilities that are available at Chicago Lying-in Hospital the performance of the test would as yet be of considerable difficulty. The actual determination of glucuronidase, as I understand it, depends upon a calorimetric method which is not difficult. Obtaining the substrate upon which that reaction is based is, however, very complicated. I am informed that the method is to feed rabbits phenolphthalein and collect the urine over a period of days, and from that urine there is then extracted a phenolphthalein glucuronidate which is purified by a number of processes so that other excretory products are eliminated. It is only then that one has available a substrate on which the test can be performed. I point out that these operations are now extensive and that phenolphthalein glucuronidate will undoubtedly soon be commercially available either as a biologic product or as a synthetic product. When that time comes a great many more of us can undertake such studies, and increased information concerning their value will rapidly become available.

DR. ODELL (Closing).—The test for beta-glucuronidase was originally designed for use in cancer. Patients with cancer have some increase in tissue level, although not consistently so. To date there have been no conditions giving as high serum values as pregnancy, or toxemia of pregnancy.

The reason for the increase in serum enzyme concentration during pregnancy and toxemia of pregnancy should become of considerable interest. We analyzed the vital organs of two women expiring near term. The enzyme concentration of these tissues gave no clue as to origin. Since the highest concentration in the blood lies in the buffy coat, future investigation may lie in that direction.

FACE PRESENTATION*

A Study of 160 Cases

JOSEPH W. REDDOCH, M.D., NEW ORLEANS, LA.

(From the Departments of Obstetrics and Gynecology, School of Medicine, Tulane University of Louisiana, and Charity Hospital)

LITTLE has been written, especially in America, concerning the problems of face presentation, although the dangers of, and consequences from, mentoposterior deliveries are generally recognized and feared. The scant literature is evidence of the lack of experience that the clinical observer has had with this condition. Obstetric centers have been somewhat remiss in reporting their accumulated results in its management, and the greater part of present-day thought and teaching has been dictated by the eminent obstetricians of the nineteenth century. Reports of several small series have appeared in recent years, and the authors have set up the results obtained in these few cases as examples for the management of the condition in general.

A brief résumé of the literature reveals that, in 1941, Mussio and Walker[1] suggested that conversion of mentoposteriors to vertex occiput anteriors was the safest form of delivery for the mother and child, and gave as their reason for this opinion the maternal mortality of 11.6 per cent obtained by Reed in 1905, with an infant loss of 40.6 per cent in this position. On the other hand, DeLee[2] concluded that "mentosacral positions terminating happily for the mother and child are so exceedingly rare that, for practical purposes, it is best to consider them absolutely impossible and as always requiring interference from art." That untoward complications are not infrequent in face presentations is given further evidence by the report of Gill,[3] in 1944, of dystocia caused by a forelying elbow. The most comprehensive recent study of face presentations is the series compiled by Posner and Buch,[4] in 1943, in which 87 cases were reported from the Harlem Hospital. They concluded that, because of the "high maternal and fetal morbidity and mortality and the greater incidence of disproportion and prolonged labor with dystocia accompanying extension of the head, cesarean section should be given greater consideration than heretofore in early diagnosed cases of face presentation, especially in primiparae."

This report will be concerned with the results obtained in 160 cases which occurred on the combined services of the Charity Hospital of Louisiana, in New Orleans, during the twenty-five years ending with December, 1946. The total number of deliveries during this period was 88,114, making an incidence of face presentations of 0.184 per cent, which compares with 0.19 per cent reported by Posner and Buch,[4] and 0.25 to 1 per cent generally given as the incidence in most texts. This incidence is comparable to that found by Kemp,[5] in 1859, when he reported two cases in an analysis of 1,000 deliveries occurring in Baltimore.

*Read before the Central Association of Obstetricians and Gynecologists, Louisville, Kentucky, Oct. 23-25, 1947.

The purpose of this study is to analyze the comparative results obtained by the several methods that have been used in the management of this presentation, in the hope of deducing from it a sounder policy for handling this relatively uncommon, but often difficult, obstetric problem (Table I).

TABLE I. FREQUENCY

	AUTHOR'S SERIES	HARLEM HOSPITAL SERIES	COMBINED SERIES
Total deliveries	88,114	48,000	136,114
Face presentation	160	87	247
Incidence	0.184	0.19	0.187

Table II gives age and parity for the series and shows that the condition is about three times as frequent in multiparas as in primiparas, the ratio being 119 to 41, respectively. It is also seen that in patients 20 years of age or younger, it occurs much more commonly in primiparas (24 cases) than in multiparas (13 cases) a ratio of 2 to 1; between the ages of 21 and 30 years, in 82 cases, there were 13 primiparas and 69 multiparas, a ratio of 1 to 5; and over 30 years of age, the relative frequency was 4 primiparas to 37 multiparas, a ratio of 1 to 9.

TABLE II. AGE AND PARITY

	PRIMIPARAS	MULTIPARAS	TOTAL
20 years or less	24	13	37
21-30 years	13	69	82
31 years and over	4	37	41
Total	41	119	160

The frequency of the various positions is shown in Table III. Engagement was in the right oblique diameter in 82 cases (65 left mentoanteriors and 17 right mentoposteriors), while in 45 cases it was in the left oblique diameter (18 left mentoposteriors and 27 right mentoanteriors). Transverse position and those in which the position was not diagnosed accounted for 33 cases. The ratio of primiparas to multiparas for the various positions paralleled the incidence of each in the series except in mentoposteriors, which accounted for 35 cases, of which 15 were primiparas and 20 multiparas.

TABLE III. POSITIONS

	PRIMIPARAS	MULTIPARAS	TOTAL
Left mentoanterior	12	53	65
Left mentotransverse	3	5	8
Left mentoposterior	8	10	18
Right mentoanterior	3	24	27
Right mentotransverse	0	6	6
Right mentoposterior	7	10	17
Position not stated	8	11	19
Total	41	119	160

Etiology

In reviewing the records, wherever possible, either by inference or by an actual note, an effort was made to arrive at some conclusion as to the cause of the presentation. The results of this tabulation are found in Table IV. Contrary to the findings of others, contracted pelvis was the chief etiological factor in only 6 cases and a large baby accounted for 8 more, making a total of 14 cases in which disproportion could be considered the principal factor in the causation

of the presentation. It is noteworthy that 52 of the cases occurred in women where parity (fourth or more pregnancy) was a major factor, and that 9 cases were anencephalic monsters, and 12 followed primary brow presentations. There were 56 cases, 22 being primiparas, in which no reason was evident for the presentation. This is at variance with Beck,[6] who states that in his experience he has seen only one primary face presentation.

TABLE IV. ETIOLOGY

	PRIMIPARAS	MULTIPARAS	TOTAL
Parity only (4th baby or more)	0	43	43
Parity with another factor	0	9	9
Hydramnios	0	1	1
Compound presentation	1	2	3
Second twin	1	0	1
Secondary to brow	4	8	12
Cord about neck	0	2 (brow)	2
Small babies*	4	14	18
Large babies	2	6	8
Uterine tumor	0	1	1
Marginal placenta previa	0	1	1
Not explained	22	34	56
Pendulous abdomen	0	4	4
Small pelvis	4	2	6
Incompressible pyelitis†	1	0	1
Monster	3	6	9
Following bag induction of labor	0	1	1

*Two 6 month fetuses weighing less than 5½ pounds.
†Porro section.

Dilatation of the Cervix

Dilatation of the cervix was obtained, as is shown in the following table (Table V) in 152 cases, where delivery was per vaginum:

TABLE V. DILATATION OF CERVIX

	PRIMIPARAS		MULTIPARAS		TOTAL
Average spontaneous (0-24 hours)	27		94		121
Long spontaneous (24 hours or longer)	6	2 RMA 2 LMA 1 LMP 1 Not stated	14	7 LMA 2 RMT—10 days 3 RMP 1 RMA 1 Not stated—impacted face with foot	20
Duration not stated	1	(RMP)	2	(LMA)	3
Duhrssen's	1	(LMA—bag failed)	0		1
Bag	1	(LMP)	3	(2 LMA) (1 LMP)	4
Manual dilatation	1	(LMA)	1	(LMT)	2
Breech (Braxton Hicks' version)	0		1	(LMA)	1

Of the 27 cases where dilatation was delayed or obtained by operative means, 14 in 92 (15 per cent) were mentoanteriors, 7 in 35 (20 per cent) were mentoposteriors, and 3 in 14 (21 per cent) were mentotransverse, and in 3 cases, the position was not stated. It appears, therefore, that the fetal position had little effect on the ease with which dilatation was obtained.

Methods of Delivery

Several separate methods or combinations were employed in the delivery of the babies:

1. *Spontanous as Face Presentation.*—(Infant mortality, 14.3 per cent, maternal mortality, 0.) Eighty-six cases delivered spontaneously as a face, either relatively easily or following a difficult labor. Thirteen were primiparas who ended with 3 monsters, 1 macerated fetus, and 2 in which the death was not explained, an incidence of infant death of 2 in 9 viable babies. Among the 73 multiparas, there were 1 macerated fetus and 3 monsters. Of these 69 babies alive before birth, 5 died either because of, or during, labor (one being a 6-month fetus), and 5 others died before the mother was discharged from the hospital. The total gross infant mortality for the entire spontaneous group was 12 (15.6 per cent), and the corrected 10, or a corrected infant mortality rate of 14.3 per cent. This is shown in the following table:

TABLE VI, A. SPONTANEOUS DELIVERY—86 CASES

	PRIMIPARAS	MULTIPARAS
Total number of cases	13	73
Monsters	3	3
Macerated babies	1	1
Babies died at birth	0	5 (1 six-month fetus)
Neonatal deaths	2	5
Gross infant mortality	5 in 12 39%	14 in 73 19.1%
Corrected infant mortality	2 in 9 22%	9 in 68 13.2%
Positions (exclusive of 6-month fetus)		
Left mentoanterior	2	36
Left mentotransverse	1	2
Left mentoposterior	4	8
Right mentoanterior	2	21
Right mentotransverse	0	1
Right mentoposterior	1	0
Position not stated	3	5
Average corrected infant mortality was 14.3 per cent		

2. *Low Forceps to the Face.*—(Infant mortality, 12.5 per cent, maternal mortality, 0.) This operation was employed 16 times (8 primiparas and 8 multiparas). The results of this form of delivery are shown in the following table:

TABLE VI, B. LOW FORCEPS TO FACE—16 CASES

	PRIMIPARAS	MULTIPARAS
Total number of cases	8	8
Babies dying at birth	2	0
Neonatal deaths	0	0
Gross infant mortality	25%	0
Corrected infant mortality	25%	0
Positions:		
Left mentoanterior	4	5
Left mentotransverse	1	0
Left mentoposterior	1	0
Right mentoanterior	1	1
Right mentotransverse	0	0
Right mentoposterior	0	2
Position not stated	1	0
Corrected infant mortality for low forceps group was 12.5 per cent		

3. *Flexion of Head.*—(Infant mortality followed by high forceps, 40 per cent, by other methods, 0; maternal mortality, 0.) Flexion of the head was done in 15 cases, followed by spontaneous delivery in 5. Table VI, C shows the results where flexion was used, followed by spontaneous and forceps delivery.

The average corrected mortality in this group of cases was 14.3 per cent. Flexion was tried unsuccessfully in 16 additional cases which were delivered by some other method.

TABLE VI, C. FLEXION OF HEAD—15 CASES

FLEXION DELIVERIES	TOTAL NO. OF CASES		POSITIONS	INFANT MORTALITY	CORRECTED MORTALITY
	PRIMIPARAS	MULTIPARAS			
Spontaneous	1	4	1 right mentopost. 1 left mentotrans. 1 left mentoant. 1 right mentotrans. 1 not stated	0	0
Low forceps	2	1	1 right mentopost. 1 left mentopost. (macerated) 1 left mentoant.	1	0
Midforceps (Scanzoni)	0	2	2 right mentoant.	0	0
High forceps	0	5	4 right mentopost. 1 not stated	2	40%

4. *Midforceps to the Face.*—(Infant mortality, 0, maternal mortality, 0.) This was used on one primipara (left mentoanterior) where flexion had failed, and resulted in a live baby.

5. *Version and Extraction.*—(Infant mortality, 53.3 per cent; maternal mortality, 3.5 per cent.) Version and breech extraction were employed in 27 cases. The results are shown in Table VI, D.

TABLE VI, D. PODALIC VERSION AND BREECH EXTRACTION—27 CASES

	PRIMIPARAS	MULTIPARAS
Elective	7—1 easy, 6 difficult 2 RMP 1 LMA 1 LMP 3 Not stated	10—4 easy, 6 difficult 4 LMA 1 LMP 2 RMT 2 RMP 1 Not stated
After failure of flexion or/and forceps	4 { 3 LMA 1 RMP	6 { 2 LMA 2 LMT 1 LMP 1 RMP
Total	11	16
Gross infant mortality	9 (1 macerated)	6
Corrected infant mortality	8 in 10 80 per cent	6 in 16 37.5 per cent
Average corrected mortality for primiparas and multiparas—53.3 per cent		

In one multipara and two primiparas there was evidence of fetal distress before beginning the operation. In the former, flexion and forceps were tried unsuccessfully and the heart tones were 170+ per minute. In the first primipara,

a bag had been used to obtain dilatation, high forceps had failed, and the heart tones were also 170+ per minute; in the second primipara the fetal heart was irregular and flexion had also failed. In a third primipara, the baby had been dead for some time before the operation was begun. The remainder of the babies were in good condition at the time the versions were undertaken.

The length of labor in these cases varied, as is shown in Table VI, E.

TABLE VI, E. DURATION OF LABOR IN 27 VERSION DELIVERIES

		BABIES LIVED		BABIES DIED		TOTAL
Less than 10 hours	Primiparas	1	(2nd twin)	1	(difficult labor)	2
	Multiparas	1		3	(1 membranes ruptured 3½ hours)	4
11-20 hours	Primiparas	1	(right mento-posterior)	5	(3 2nd stage, 7 lb. 6 oz., 5 hours) (1 poor condition, 2nd stage 2½ hours) (1 macerated)	6
	Multiparas	5		1		6
Over 21 hours	Primiparas	0		2	(1 difficult 28½ hour labor) (1 difficult 48 hour labor)	2
	Multiparas	3	(1 mentosacral and prolapsed foot)	1	(2nd 5 hours, membranes ruptured short time)	4
Time not stated	Primiparas	0		1		1
	Multiparas	1		1		2

In four primiparas, the membranes had been ruptured for 5, 8, 10, and 48 hours before the version was attempted, ending with 3 stillborn babies and one baby in poor condition, who later died. In another primipara, the membranes had been ruptured 12 hours without complete dilatation; following accouchement forcé, a version and extraction were done, resulting in a dead baby, the mother also dying of sepsis after twenty-five days. In one multipara, after the membranes had been ruptured for nine and one-half hours, a difficult version netted an infant with intracranial hemorrhage, who lived, following several spinal punctures. In two primiparas, the membranes were ruptured two hours or less, and resulted in living babies, while two babies were lost in the three multiparas in whom the membranes had been ruptured for this duration of time. There were one primipara and one multipara in whom the membranes were ruptured for two to three hours before the version was attempted and both babies died. In the cases of three primiparas, the duration of the time of rupture of membranes before the version and extraction was not stated. They yielded a macerated fetus and two stillbirths, while two babies were dead at delivery in the 7 multiparas belonging to this group.

6. *Cesarean section.*—(Infant mortality, 0, maternal mortality, 0.) This method of delivery was used in 8 cases, 4 primiparas and 4 multiparas. All the mothers and babies survived. In one primipara, a cesarean hysterectomy was done because of an incompressible pyelitis in an ectopic kidney. The postoperative course in this case was stormy. Of the three other primiparas, two had elective sections and the other, with a small pelvis, was sectioned after an unsuccessful trial of labor. One multipara with a small pelvis was sectioned after a trial; two were repeat sections; and in another, which began as a brow presentation, a section was done when labor failed to progress after thirteen hours.

7. *Manual Rotation.*—Manual rotation followed by low forceps was used in one multipara, a right mentoposterior, in whom the membranes were ruptured at the time of the procedure. The condition of the baby and mother was good.

8. *Monsters.*—(Infant mortality 100 per cent, maternal mortality, 0.) Of the 3 primiparas and 6 multiparas who had anencephalic monsters, delivery was difficult in 3 of the multiparas. Low forceps were used in one, Braun's hook about the neck of the second, and a cephalic manual extraction was done on the third. The remainder were spontaneously delivered.

9. *Craniotomy.*—(Infant mortality, 100 per cent, maternal mortality, 33⅓ per cent.) Three multiparas were delivered by this destructive method. In one, a right mentotransverse, the patient had been in labor for ten days when she was admitted with a temperature of above 100.4 F. On admission, the heart tones were normal. Thirty hours after the membranes ruptured, however, the craniotomy was done. The second case was a grand multipara (para viii, gravida ix) with a right mentoposterior, who, after 32 hours of labor, went into shock following a sacral block. The death of the baby in this case was considered as being due to anoxia. The third case was admitted with a temperature range of 101° to 103° F., the membranes ruptured. After forty-eight hours of labor, the heart tones disappeared. The cervix was only partially dilated and the head was impacted, necessitating the craniotomy. This patient died of peritonitis on the sixth postpartum day.

Anesthesia

It was not possible to give an anesthetic in 24 cases, in which delivery occurred sooner than expected. The majority of the remaining cases were anesthetized with chloroform or ether, the latter, either alone or in combination with ethylene or nitrous oxide. Generally, the more difficult the operative procedure, the more profound the anesthetic.

Maternal Morbidity*

The following table (Table VII) gives the maternal postpartal course.

Two points are outstanding in the morbidity study: First, the more complicated the delivery, the more morbid the patient. Almost 50 per cent of those having versions and extractions and high forceps following flexion were morbid,

TABLE VII. MATERNAL MORBIDITY

	MORBID		NOT MORBID		NOT STATED	
	PRIMIPARAS	MULTIPARAS	PRIMIPARAS	MULTIPARAS	PRIMIPARAS	MULTIPARAS
Methods of delivery:						
Version and extraction	7	5	3	11	1	0
Low forceps	1	6	9	4	0	0
High or midforceps	2*	1	0	2	0	1
Spontaneous delivery and other	3†	11	10	70	0	0
Cesarean section	2‡	0	1	4	0	1
Craniotomy	0	3	0	0	0	0
Total number of cases	15	26	23	91	1	2
Long labor	5	8	3	11	0	0

*One Dührssen's and 1 flexion.
†One third degree tear.
‡One Porro section.

*In determining morbidity, the standard set up by the American Committee on Maternal Welfare was used.

while less than 20 per cent of the spontaneous deliveries for both primiparas and multiparas ran a temperature elevation. Second, one-third of the morbid primiparas and multiparas had labors that lasted twenty-four hours or longer, while in the nonmorbid group, approximately one-eighth of each had labors of this duration. Two cesarean sections in primiparas were followed by a temperature elevation; one was the patient with the ectopic kidney, who had the Porro section. Two of the three patients having craniotomies were morbid for 3 to 14 days each and recovered, while the third one died of sepsis six days after the delivery. The remainder of the morbid cases ran a slight to marked temperature elevation for 1 or 2 days to as long as 25 days.*

There were 11 postpartum patients (3 primiparas and 8 multiparas) who bled excessively or were in shock. Of these, 5 (2 primiparas and 3 multiparas) were delivered by version and breech extraction; 2 had high forceps (1 primipara and 1 multipara, the primipara following Dührssen's incisions); 3 multiparas were delivered by craniotomies; and one multipara delivered spontaneously.

TABLE VIII. POSTPARTUM HEMORRHAGE AND SHOCK—11 CASES

	PRIMIPARAS	MULTIPARAS
Version and extraction	2 (1 manually dilated cervix)	3
High forceps	1 (Dührssen's)	1
Craniotomy	0	3
Spontaneous delivery	0	1
Total	3	8

TABLE IX. CERVICAL AND PERINEAL LACERATION

	PRIMIPARAS		MULTIPARAS	
Cervix	1	(Version and extraction, manually dilated cervix)	7	3 spontaneous deliveries 2 version and extraction 1 high forceps, long labor 1 craniotomy
Perineum	7	1 first degree: version and extraction 3 second degree 1 spontaneous delivery 2 version and extraction 3 third degree 2 version and extraction 1 high forceps, Dührssen's incision	17	11 first degree 1 high forceps 10 spontaneous delivery 5 second degree 1 craniotomy 2 version and extraction 1 high forceps 1 third degree: spontaneous delivery

Maternal Mortality

Two mothers were lost in the 160 cases. The first, in 1929, was a Negro gravida 4, with a mentoposterior, who was admitted in labor several days after the membranes had been ruptured. The temperature on admission was 100° to 101° F. At the end of forty-eight hours, the cervix was almost completely dilated and the face was impacted in the mentosacral position. The uterus was tightly molded about the baby. A craniotomy was chosen for the delivery. The patient died six days later of puerperal sepsis and general peritonitis. The second maternal death was one of the cases in 1934, a 20-year-old Negro primipara with an adequate pelvis, who was admitted in labor. After seventeen hours of

*One patient, who had a version and extraction following manual dilatation, died on the twenty-fifth day.

labor, the membranes ruptured, and an arm prolapsed, complicating the left mentoanterior position This was followed by evidence of fetal distress. The cervix was undilated; a manual dilatation was attempted followed by a version and extraction, using nitrous oxide only for the anesthetic. The baby could not be revived. The mother became septic, developed a right femoral thrombophlebitis, and died on her twenty-fifth postpartum day.

The first case probably was handled as conservatively as the 1929 armamentarium would have permitted, unless a Porro section had been used, but the second case is a striking example of poor obstetric management and violates the conditions needed for successfully doing versions and extractions. With penicillin, sulfonamides, and streptomycin, as well as improved technique, a section on either of these cases would have been safer, employing a hysterectomy on the first and the extraperitoneal technique on the second.

Condition of Babies

The conditions of the babies at birth are shown in Table X, while Table XI summarizes the infant loss, and Table XII outlines fetal abnormalities in living babies found at birth.

One multipara finally delivered a live baby with low forceps, after twenty-four hours, the face being traumatized. The baby of another multipara was alive but had a marked cleft palate and harelip. A third multipara, after twenty-two hours of labor, delivered a normal baby with edema of the glottis. The position in this case was a left mentoposterior. In still another multipara, following a version and extraction, the baby had a fractured clavicle; while the baby of

TABLE X. CONDITION OF INFANTS IN TYPES OF DELIVERY

	LIVING		STILLBIRTH		NEONATAL		MACERATED		MONSTER	
	PRIMIPARAS	MULTIPARAS	PRIMIPARAS	MULTIPARAS	PRIMIPARAS	MULTIPARAS	PRIMIPARAS	MULTIPARAS	PRIMIPARAS	MULTIPARAS
Mid and high forceps	1	5	0	2	1	0	1	0	0	0
Version and extraction	4	11	6	5	1	1	1	0	0	0
Spontaneous delivery	10	69	0	5	1	2‡	0	3‖	3	6¶
Low forceps	10*	8	0	1	2†	0	1§	0	0	0
Cesarean section	4	4	0	0	0	0	0	0	0	0
Long labor	5	15	2	4	0	0	1	0	0	0

*One followed version.
†One premature.
‡One 2½ pound baby; 1 6-month pregnancy.
§Head flexed.
‖One hydramnios; 1 4 pounds.
¶Three difficult deliveries.

TABLE XI. INFANT MORTALITY

	PRIMIPARAS	MULTIPARAS
Total number of babies	41	119
Less monsters, macerated, and prematures	5	11
Net viable	36	108
Fetal loss at delivery and during neonatal period	10 (27.7 per cent)	15 (13.9 per cent)
Percentage loss: viable babies, 17.3 per cent		

TABLE XII. ABNORMALITIES IN LIVE BABIES AT BIRTH

Trauma to face	1 (para iv, 24½ hour labor, LMA, low forceps, baby lived)
Fractured clavicle	1 (para iii, 3½ hour labor, version and extraction under ether, baby lived)
Hair lip, cleft palate	1 para ii, LMA, spontaneous delivery 7½ hour labor, baby lived)
Severe moulding head	1 (para ii, RMA, spontaneous delivery 37½ hour labor, baby lived)
Face markedly cyanotic	3 (para ix, RMA, spontaneous delivery 40 hour labor, baby lived; para i, LMA 21+ hour labor; para iv, RMP spontaneous delivery
Edema of glottis	1 para vi, LMP, spontaneous delivery 9 hour labor, baby lived)
Intracranial hemorrhage*	1 (para i, gravida iv, elective version in RMP
Condition poor (asphyxia)	1 (para 0, LMA, version and extraction following bag)

*Several other babies in the later neonatal period exhibited signs of intracranial hemorrhage while their immediate postpartum condition was poor.

a fifth multipara, delivered by version and extraction, had an intracranial hemorrhage, but survived after receiving several cysternal and spinal taps. Although none of the abnormalities listed were permanent (except the lip-palate imperfection) any one of them could have been associated with a fetal intracranial hemorrhage, or a lifelong disabling deformity might have resulted.

Discussion

A. *Incidence.*—It appears that the incidence of face presentations stated in our obstetric texts is too high and probably should be revised. Although that found in this series compares with that of others, it is possible that a number of cases beginning as face were converted into vertex, the original presentation being forgotten.

In this series there were 92 (57.5 per cent) mentoanteriors, 35 (22 per cent) mentoposteriors, 13 (9 per cent) mentotransverse, and 13 (12 per cent) in which the position was not stated, which compares with 50.3 per cent, 23 per cent, 13 per cent, and 14 per cent respectively reported by Posner and Buch.

B. *Etiology.*—Disproportion, although present in 14 cases, did not play a major role in the production of the presentation, which is at variance with general opinion and the incidence of 2 out of 3 cases, as given in the Harlem report. Multiparity does seem to play a major role and occurred alone or in combination with other factors in 52 cases. Of this number, 14 patients were grand multiparas, having their seventh to fifteenth baby. Brow presentations preceded complete extension of the head in 12 cases. Other factors, such as pendulous abdomen, fetal neck tumors, hydramnios, placenta previa, small babies, compound presentation, and the use of the hydrostatic bag in the first stage of labor, probably do predispose to face presentation and their presence should

keep one alert for this condition, although in this series their occurrence was infrequent.

C. *Management.*—Early diagnosis is important. In the majority of these cases, the diagnosis was made after labor was well advanced, yet several were diagnosed before the onset of labor. Primary face presentations should be recognizable by careful abdominal palpation and vaginal examination, confirming if necessary by x-ray. The important findings are concave dorsal plane, prominent small parts, loud fetal heart tones heard best through the anterior fetal chest wall, and the presence of a marked cephalic prominence on the same side of the baby as is the back; vaginally, the facial features are not to be confused with the breech. This, combined with multiparity, especially grand multiparity, disproportion, and other more or less uncommon conditions, should lead to an earlier diagnosis and, therefore, a less complicated labor and delivery.

Labor should be conducted guardedly and aseptically, for many face presentations are potential candidates for cesarean section. Fluids, sedation, and care of the bladder and rectum are more important than in vertex presentations. The first stage of labor is likely to be prolonged; the longest in this series was 10 days, ending with a craniotomy.

Since spontaneous delivery does occur in all positions, it should probably be anticipated if there is no disproportion, but interference (low forceps to face or following flexion, midforceps to face, flexion alone, and manual rotation) should always be kept in mind as a possibility for a safe termination of labor. Early flexion of the head in mentoposteriors, under anesthesia and aseptic technique, is probably preferred in multiparas and an occasional primipara, allowing labor to progress normally afterward. The Schatz, Ziegenspeck, and Thorn maneuvers may be useful. Failing to accomplish flexion, cesarean section is infinitely better than to attempt delivery by the breech.

This last method is the least desirable of all methods for delivery. Although it was used in this series in 10 cases where other methods failed, the fetal results were almost as poor when done electively. The attitude of the fetus, duration of labor, and the possibility of long-standing ruptured membranes presage an unhappy ending for the baby and danger to the mother, and predispose to violation of the conditions under which this operation may be expected to be successfully done. Delivery of one second twin in this series by elective version and extraction was apparently justified. Perineal and cervical tears, hemorrhage, sepsis, damage to the living fetus were most common in the cases where this operation was done. One of the maternal deaths was due directly to this method of delivery, where poor judgment was noted and obstetric hysteria was evident. Certainly, waiting or cesarean section could have produced no worse results.

The suggestion made by Posner and Buch[4] that cesarean section should be done more often, especially in primiparas, is borne out by the results herein reported, and should be made to include (1) face presentations in multiparas having more than the fifth or sixth baby, (2) any case where the first stage is not progressing satisfactorily, (3) when conditions found during the second

stage are not favorable, rather than taking a chance with the two lives involved. The availability of sulfonamides, antibiotics, and the extraperitoneal cesarean technique makes conservatism justifiable in the remainder of the cases. This should eliminate the necessity of craniotomies and other mutilating operations. However, death of the fetus in utero and fetal deformities are direct contraindications to this policy and must be eliminated before subjecting the patient to the danger of a cesarean section.

It should be borne in mind that the long labors and difficult operative procedures necessitated by face presentations for vaginal delivery are the chief causes of maternal hemorrhage and infection and fetal death. In at least one case, the baby died during the long labor and was ultimatedly delivered vaginally.

The anesthetic did not seem to play an important part in the delivery, except when a formidable procedure was undertaken. Version and extraction, high and midforceps, and craniotomies required deeper anesthesia than spontaneous and low forceps deliveries. That this was the case is in line with what would be expected.

Summary and Conclusions

1. The results obtained in the delivery of 160 cases of face presentation are reported.

2. The frequency of face presentation in this series was 0.184 per cent, which is comparable to 0.19 reported in a recent series. Multiparas were three and a half times more common than primiparas and mentoanteriors were more often seen than other positions.

3. Parity and its accompanying lack of abdominal and uterine tone were the most important etiological factors. However, other conditions must be borne in mind as possible causes, and the presentation should be watched for in contracted pelves and in patients with large babies. It appears that primary face presentations are not uncommon, there being 56 cases in 160, in which no explanation could be found for the presentation.

4. Spontaneous delivery occurred from all positions and may be anticipated provided there is no disproportion in most multiparas and possibly a few primiparas. In the latter group, cesarean section should be done electively when the diagnosis is clear, after fetal death and deformities incompatible with life have been eliminated. Low forceps to the face or following flexion of the head and manual rotation may be needed to finish the delivery late in the second stage. Versions and extractions should have no place in the delivery of face presentations except in an occasional case of a second twin which presents as a face.

5. The adjusted infant mortality for this series was 17.3 per cent, which could be materially reduced by more carefully watched first and second stages, omission of complicated vaginal procedures when simple procedures failed, and substitution of cesarean section in these cases.

References

1. Mussio, John G. E., and Walker, Howard L.: Am. J. Obst. & Gynec. 41: 88-92, 1941.
2. DeLee, Joseph B., and Greenhill, S. P.: Principles and Practice of Obstetrics, ed. 9, Philadelphia, 1947, W. B. Saunders Company, p. 551.
3. Gill, John Joseph: Am. J. Obst. & Gynec. 48: 133-134, 1944.
4. Posner, A. Charles and Buch, Irwin M.: Surg., Gynec. & Obst. 77: 618-630, 1943.
5. Kemp, William M.: Obstetrical Notes Based on 1000 Cases of Delivery, Am. Med. Monthly 12: 161-190 (September), 1859.
6. Beck, Alfred C.: Obstetrical Practice, ed. 3, Baltimore, 1942, The Williams and Wilkins Company, p. 371.

Discussion

DR. HENRY BAUXBAUM, Chicago.—The greatest value one can receive from a presentation of this kind is a comparative evaluation of the various methods for handling this fairly rare and difficult complication, to employ the method which gives the greatest possibility of success. Dr. Reddoch gives us the results of his arduous studies and makes several pertinent observations. Just to re-emphasize a few of his suggestions: Cesarean section as an elective procedure is becoming more popular in the management of face presentation and rightly so. This operation is particularly indicated in elderly primigravidas, and in cases of cephalopelvic disproportion and persistent mentoposterior presentation. This procedure carries a greater assurance of safety to the mother, as well as a greater fetal salvage, as shown in his tables. Version is extremely difficult as well as quite dangerous to perform in a face presentation, because of the marked extension of the fetal body with the location of the buttocks high in the fundus. The value of x-ray in confirming the diagnosis is unquestionably of great value, as well as to rule out the possibility of a fetal deformity, if a cesarean section is contemplated. I believe that, inasmuch as mentoposterior is an impossible delivery, and may result in an obstetric tragedy if neglected, it is best treated by a cesarean section if the cervix is not dilated, or a conversion, if the condition is recognized after the cervix is completely dilated and effaced. The conversion is done under a deep either anesthesia, after which the patient is allowed to wake up, and labor is permitted to continue until the head molds and dips down deep into the pelvis.

For the purposes of comparison, I would like to refer to the results from the service of the Chicago Maternity Center of face presentation for the past ten years. First, I want to call to your attention the fact that all our cases are conducted in the patient's own home under adverse sanitary conditions. All cases are conducted by an interne who is supervised by a resident, and if necessary an attending physician is summoned. If the delivery is impossible to complete in the home, the patient is hospitalized.

In the period from 1937 to 1946 inclusive, there were 22,440 deliveries, of which 58 cases were diagnosed as face presentation. This is an incidence of 1 to 387 or 0.258 per cent, a slightly smaller incidence than that cited by Dr. Reddoch. Of this group, spontaneous delivery occurred in 42 or 72.4 per cent. Spontaneous delivery following conversion occurred in 2 or 3.4 per cent, making a grand total of 75.8 per cent who delivered spontaneously. One of the latter cases developed an incomplete rupture of the uterus in the right broad ligament, with a subsequent supravaginal hysterectomy followed by recovery. Also, I wish to call attention to the high incidence of prolapse of the cord associated with this type of malpresentation. In the aforementioned 44 cases there were three prolapsed cords and one prolapsed arm. There were three low forceps, two midforceps and two high forceps, for a percentage of 12.1 per cent. Six of these seven cases were preceded by conversion and manual rotation. Version followed by extraction was done four times or in 7.0 per cent of this series. Three of these versions followed a failed conversion. The fetal mortality here was 50 per cent. Craniotomy was performed in two cases or 3.4 per cent. In one of the cases the Center was called in when the patient was fully dilated and had a threatened uterine rupture. She had been previously attended by a midwife and a private doctor. The last case was an anencephalic monster and here extraction of the fetus was accomplished with a Braun's hook, a percentage of 1.7 per cent. In this group there were 7 primiparas and 51 multiparas, a one to seven plus relationship. In spite of or because of the fact that there were no cesarean

sections in this series of face presentations delivered in the home, there was no maternal mortality. Our gross fetal mortality was 27.58 per cent, due to twelve stillbirths and four neonatal deaths. If we count out five anencephalic monsters, two cases in which there were no fetal heart tones audible on arrival of our doctors, and two previable babies under 1,500 grams, our fetal mortality was 12.06 per cent, approximately the same as those of Dr. Reddoch. There were five fetal monstrosities out of 58 cases, a little less than 10 per cent which was the prime etiological factor in the causation of this condition, the so-called snout presentation.

DR. E. L. KING, New Orleans, La.—We have had several cases, both in the hospital and private practice, that have been diagnosed as primary presentation of the face before labor started, but this diagnosis cannot always be made. The x-ray has proved extremely valuable in helping this diagnosis and also in the matter of ruling out an anencephalic monster.

I agree with Dr. Reddoch that more frequent resort to cesarean section in properly selected cases is in order, and I would include in that all cases of face presentation in primigravidas.

DR. RUDOLPH W. HOLMES, Charlottesville, Va.—In the normal, and as well in flat pelves, the characteristic descent in labor is with the chin directed to the side—i.e., the mentobregmatic line is placed transversely; the molding of the head produces a temporary dolichocephalia, and the less the skull bones have ossified, the more marked is such development. Further, the chin will not rotate to the front until the elongated hind head has passed the promontory; therefore, rotation may be so delayed that the mouth may be visible before rotation takes place. This phenomenon of labor in fact is so characteristic, that rotation with forceps never should be assayed until the chin appears under the pubes, from spontaneous rotation. A face presentation, chin at the promontory, may rotate spontaneously if left to nature; a chin in the hollow of the sacrum, likewise, may rotate 180 degrees in the natural course of labor. I have seen several of these instances. Face presentation in eutocia; overly large infants may cause dystocia.

REVIEW OF THREE HUNDRED ANTERIOR AND POSTERIOR COLPORRHAPHIES*

With a Plea for an Anatomical Correction of These Traumatic Hernias Earlier and With Presentation of Author's Procedures of Repair

W. O. JOHNSON, M.D., LOUISVILLE, KY.
(From the Louisville General Hospital)

LACERATIONS of the perineum did not escape the notice of Celceus. The first repair procedure was based on the idea of reducing the size of the vaginal canal so that it would hold the uterus in place, but it was not until 1913 that Fothergill[1] published the details of his operation on correction of genital prolapse and for the first time gave an anatomical repair approach to the operation.

A review of the anatomic relationship is brought out in the following essays: Sears,[2, 3] Hill,[4] Davies,[5] Goff,[6] Barrett,[7] Cameron.[8-10]

The pelvic structures are both suspended and supported. They are *suspended* by the ligamental folds of the peritoneum and fascia (round, uterosacral, uterovesical ligaments). They are *supported* by the pelvic diaphragm or the musculofascial floor of the pelvis (levator ani, and the perineal muscle group). They both support and complement each other and are situated one over the other in the pelvic strait.

Pelvic floor relaxations and the final result of complete prolapse of the uterus, the associated pelvic congestion, and pelvic structural changes, from beginning to end, vary only in degree, the process being essentially the same throughout.

Can we make the patient fit the operation as well as the operation fit the patient? If we are dealing with degrees of the same condition, we should strive to have a procedure that will anatomically suit the condition, and the indicated side procedures may be included at the same operative procedure. The one constant factor in all of these cases is the need for an anatomical repair of the cystocele and rectocele, which is least stressed or in some cases almost forgotten in many of the approved operative procedures. Great stress is placed on the technique of the vaginal hysterectomy and the interposition operations, but little or no emphasis is placed on the anatomical repair of the hernia,[11, 12] in the anterior and posterior walls of the vagina. Without a good foundation, how long can an architectural masterpiece stand? We are not only dealing with different

*Read before the Central Association of Obstetricians and Gynecologists, on Oct. 25, 1947, Louisville, Ky.

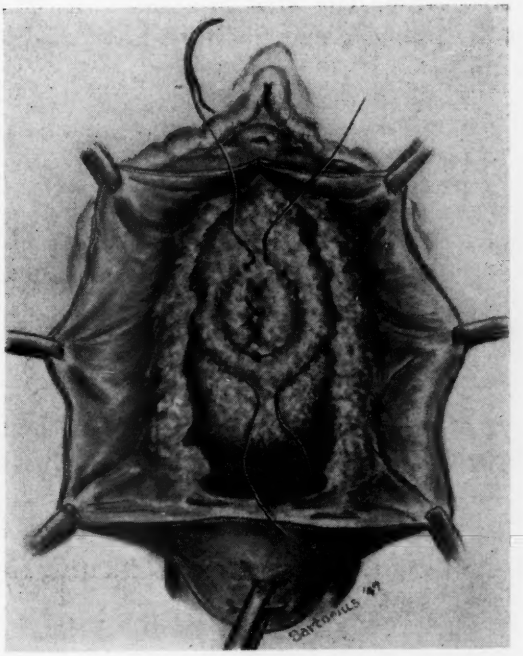


Fig. 1.—Attachment of bladder to cervix has been cut. Bladder is being advanced beneath the pubovesical fascia by purse-string sutures.

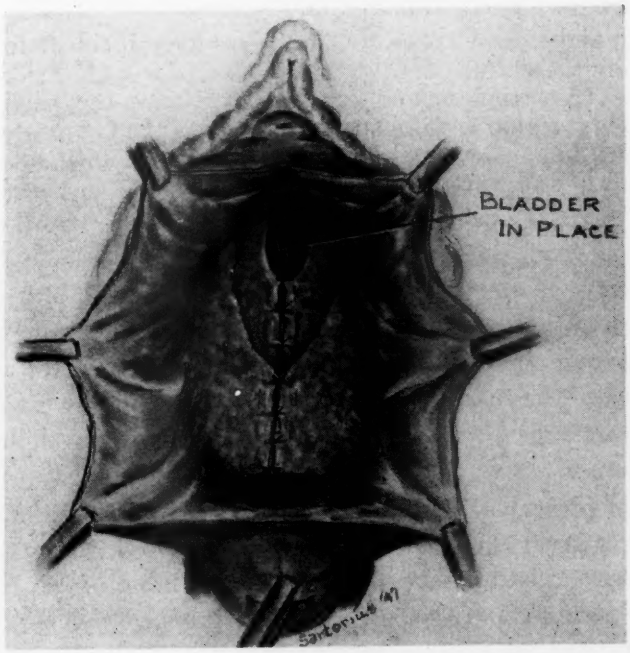


Fig. 2.—Bladder replaced in proper position. Sutures have been placed for approximation of pubovesical cervical fascia beneath bladder and to the anterior wall of the internal os of the uterus.

degrees of the same condition, but with different individuals which necessitates individualization of the problem, and the procedures used should be considered along the following lines:

1. The age and general physical condition of the patient.
2. Desirability of preserving menstruation.
3. Desirability of preserving child-bearing functions.
4. Degree of descensus and condition of supporting structures.
5. The co-existence of disease of the cervix or corpus uteri.
6. The size of cystocele and rectocele and condition of repairability of supporting structures.
7. Previous operative work.
8. "Will" of the patient to co-operate and get well.

These conditions of prolapse and descensus are not all due to "poor obstetrics," or "bad obstetrical judgment," nor to "obstetrical neglect." In many women there is an inherent defect in the development of the muscle and fascial structures that support the uterus and other pelvic and generative organs, which predisposes them to develop these debilitating conditions, as is found in the following:

1. Late onset of menstruation with persistent retroversion of uterus in constitutionally inferior women.
2. Borderline or infantile pelvic organs before their first pregnancies, followed by retroversion after pregnancies.
3. Effects of frequently repeated labors.
4. Atrophy and loss of tissue tone and elasticity incident to menopause.
5. Spina bifida occulta.
6. Traumas from tumors and other causes leave the pelvic floor and its faulty attachments unable to withstand the forces of the frequent excessive strain of coughing, sneezing, and straining with stool, etc., until all the supportive structures give way and complete prolapse results.

These unfortunate women are like the poor, "always with us." The patient is interested only in the relief of her symptoms and not in a differential diagnosis. With an insertion of properly fitted pessary, clearing up of vaginitis, relieving the congestion and teaching the patient better care of herself, she soon finds that she is on the road to improvement of her symptoms, if not a complete cure, and she must be prepared mentally as well as physiologically for the operative procedure.

We wish to present an analysis of three hundred such individuals, taking 196 charity cases from the Louisville General Hospital, the operation being in most instances supervised by the author in the training of the House Staff, and 104 private cases between 1938 and 1942. In this group there were only three Negro patients. Two hundred ninety-four of the cases were multiparous, and five charity cases and one private case were nulliparous. All of these cases had moderate to severe cystocele and rectocele and no third degree tears.

TABLE I

AGE GROUP	NUMBER	PER CENT
12-20 years	3	1
21-30 years	45	15
31-40 years	103	34.3
41-50 years	70	23.3
51-60 years	53	17.6
61-70 years	22	7.3
71-80 years	4	1.3
Total	300	99.8

Analyzing Table I, we find that 151 patients were operated upon before 41 years of age and 149 after 41 years of age, or over one-half of the patients were operated upon in the second 20 years of their lives, while the remaining half of the cases were scattered over the last 40 years of life. In only 56 of these cases were the symptoms less than a year, the shortest period being two weeks and the longest over 24 years, with an average duration of symptoms of 10.5 years before operation.

TABLE II

CHIEF COMPLAINT	NUMBER	PER CENT
"Falling out" or "bearing down sensation"	94	31.3
Pelvic or low abdominal pain	64	21.3
Backache	59	19.6
Bladder symptoms (frequency, dribbling, stain incontinence)	57	19.0
Vaginal bleeding	16	5.3
Others	10	3.3
Total	300	99.8

The great majority of the symptoms are directly referable to the pelvis, easily seen, and many times diagnosed by the patient and yet have been allowed to persist for an average of 10 years before correction. Palliative use of the pessary to confirm the diagnosis will not only give relief but will help to point out coexisting pathology if not relieved.

Orthopedic consultations should be the rule in those cases of persistent backache.

TABLE III

OTHER ASSOCIATED SYMPTOMS	NUMBER	PER CENT
Bleeding, abnormal all forms	119	39.6
Leucorrhea	112	37.3
Incontinence	81	27.0
Constipation	44	12.7
Dysmenorrhea	38	12.6
Postmenopausal bleeding	24	8.0

The striking finding in this table is the high percentage of cases of vaginal bleeding of all forms. This is the result of, or is associated with, changes in the uterus from congestion, fibroids, or chronic cervical ulceration and is due to some cases, even in the absence of the uterus, to chronic ulcerative vaginitis. The other symptoms are comparatively of little significance.

TABLE IV

COEXISTING MEDICAL COMPLICATIONS	NUMBER	PER CENT
Hypertension	64	21.3
Secondary anemia	28	9.3
Syphilis (old)	10	3.0
Early tuberculosis	6	2.0
Diabetes	3	1.0
Total	111	

A total of 111 cases or over one-third of the series had some chronic medical complication coexisting with the pelvic pathology. This tends to increase the risk and lower the chances of satisfactory end results. In addition to the medical complication, associated pathology in the uterus was as follows:

251 instances of chronic cervicitis of varying degrees.

113 had different degrees of uterine prolapse and of these, 48 had had complete prolapse at some time. In no case was carcinoma suspected before operation.

37 cases of uterine fibroids, together with the numerous vascular changes in the uterus, vagina and other pelvic structures.

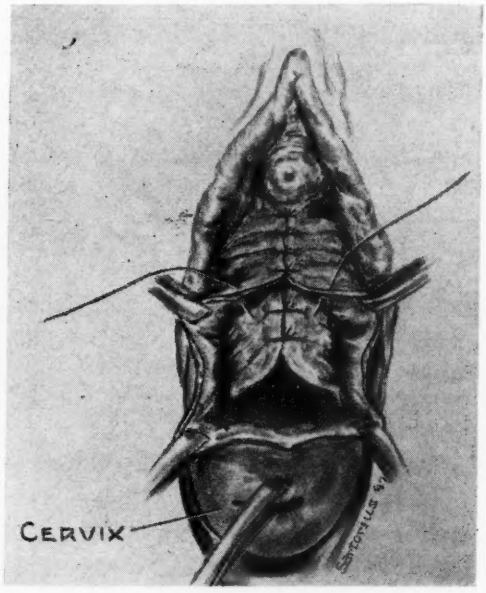


Fig. 3.—Fascia has been completely approximated over urethra and bladder. Excess anterior wall vaginal mucosa excised and edges being appr imated. Operation completed.

In every case in this series an anterior and posterior colporrhaphy was done in the following manner: An anatomical dissection and reapproximation of the structures to cure the direct traumatic hernias.

Conditions necessary for the cure of herniation of the pelvic floor:

1. Anatomical repair of pelvic floor that will give sufficient support.
2. Change the vaginal direction so that it goes from the symphysis back to the hollow of the sacrum (in an oblique direction).
3. Lessen the vaginal opening so that the walls will not prolapse through, but vaginal canal must be preserved.

4. Bladder must be properly replaced and supported.

5. Have uterus (if left in) in anterior position with support of cardinal ligament and out of line with axis of vagina.

6. Make repair before the tissues have become so fibrotic that they cannot resume normal function.

In order to correct the associated pathology, in addition to the anterior and posterior colporrhaphies, the following additional operations were done:

TABLE V

ADDITIONAL OPERATIVE PROCEDURES	NUMBER	PER CENT
Vaginal hysterectomy	156	52.0
Cervical amputations and dilatation and curettage	65	21.6
Abdominal hysterectomy	26	8.6
Dilatation and curettage and cauterization of cervix	24	8.0
Dilatation and curettage with tubal ligation, cervical amputation	18	6.0
11 patients had previous supravaginal hysterectomy operations	11	3.6
Total	300	99.8

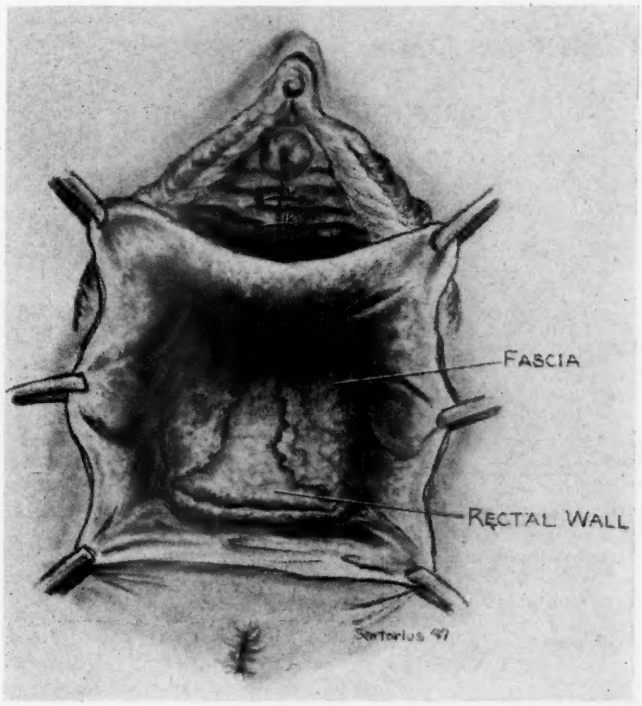


Fig. 4.—Radical repair of rectocele, showing longitudinal splits in the areolar fascia of the posterior vaginal wall.

Time does not permit a discussion of so controversial a combination of operations, but it permits a statement of a few facts: That 11 patients had had previous hysterectomy without any attempt at repair of the cystocele and rectocele. The 18 patients that had amputation of the cervix and tubal ligations were women who had large families beyond their means to care for and conservative measures were instituted rather than have the uterus removed. The

majority of the cervical amputations alone were in old women with apparently normal uteri for their age; in all cases a thorough curettage was done to see if pathology might be present and the uterus was left in place to give better pelvic support.

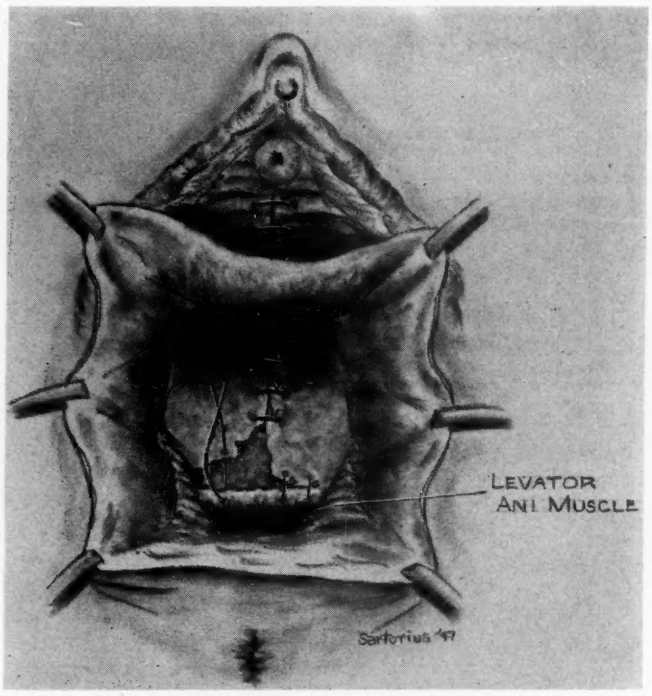


Fig. 5.—Radical repair of rectocele. The areolar fascia of posterior wall of vagina has been exposed and longitudinal split is being sutured and the transverse split of fascia with the fascia of the triangular ligaments being brought together.

TABLE VI

POSTOPERATIVE COMPLICATIONS	NUMBER	PER CENT
Pyelitis	20	6.6
Cystitis	18	6.0
Mild vaginal bleeding	11	3.6
Perineal wound infections	10	3.0
Shock	3	1.0
Thrombophlebitis	3	1.0
Pneumonia	2	6.0

There were no hospital deaths in this unselected series of 300 cases, and the complications produced by infection responded readily to sulfa and other therapy. The three cases of thrombophlebitis were mild, one not appearing until the twenty-first postoperative day and no anticoagulants or vein ligation were necessary.

The most consistent findings were chronic cervicitis and uterine vascular changes associated with the prolonged congestive state of the pelvic structures.

The three cases of carcinoma of the cervix were not suspected before operation and were followed with deep x-ray therapy. One patient with car-

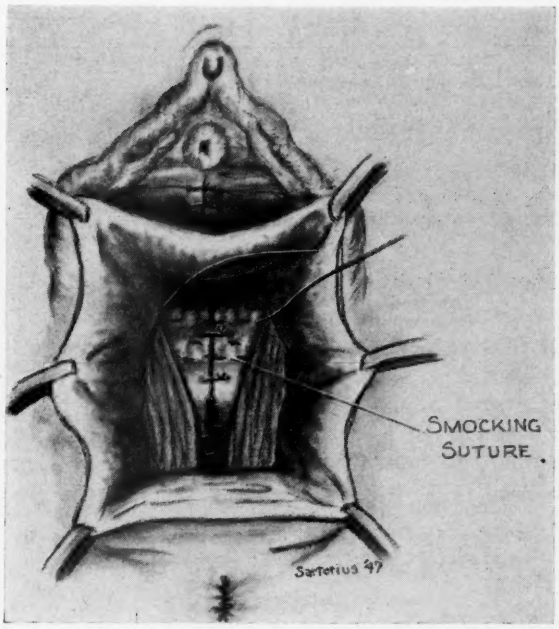


Fig. 6.—Radical repair of rectocele. Transverse laceration of triangular ligament has been approximated and redundant fascia of posterior vaginal wall is being plicated by smocking suture to close weakness of walls and to reinforce pelvic floor with fascial planes.

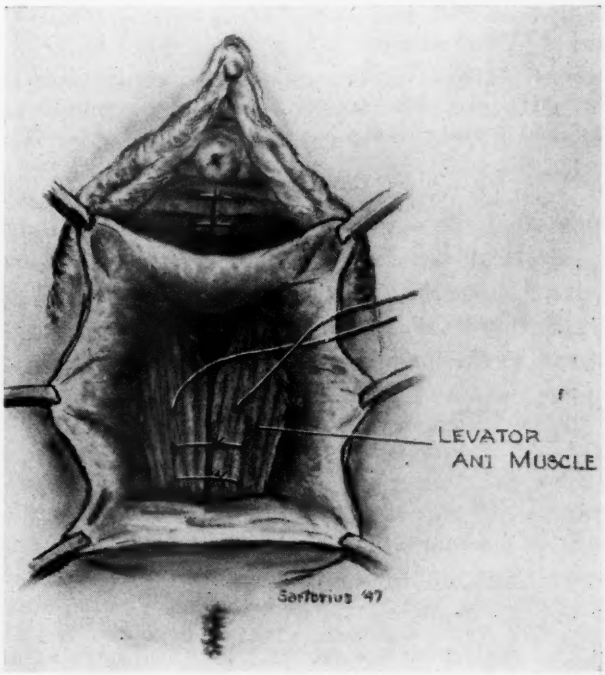


Fig. 7.—Radical repair of rectocele. The split edges of the fascial planes have been approximated and plicated and the levator ani muscles loosely approximated with catgut sutures. Mucous membranes are approximated with interrupted catgut and skin edges with subcuticular stitch of chromic catgut. At completion of operation, rectum dilated manually to admit three fingers.

TABLE VII

PATHOLOGICAL REPORTS OF TISSUE EXAMINED	NUMBER
Cervicitis	251
Fibrosis uteri or uterine vascular changes	68
Leiomyomas	37
Hyperplastic endometritis with polyps	25
Endometriosis	8
Fibroma of ovary	3
Carcinoma of cervix (early)	3
Carcinoma of fundus uteri	1

cinoma of the cervix died three years after operation even after curative doses of radium and x-ray treatment had been carried out.

The anesthesia used was 270 spinals with the majority of these associated with Pentothal analgesia. The only disagreeable reaction from the anesthesia was in five cases of spinal anesthesia in which headache appeared, but all cases cleared up in five days with lowering of the head, sedation, and daily doses intramuscularly of nicotinic acid (100 mg.).

The follow-up results in this series from six months to ten years:

Good:	230 cases—76.6 per cent
Satisfactory	45 cases—15.0 per cent
Poor:	25 cases— 8.3 per cent

Of the twenty-five patients having poor results, there were only six who had urgency incontinence. There were eight having slight recurrence of cystocele from two to five years after operation, most of them without symptoms. The remainder had subjective symptoms of backache, pelvic pain or fullness, and some dyspareunia, all referable to the pelvic structures. The average age of the patients with poor results was over 42 years; only two of the twenty-five patients were under 40 years of age.

The two patients with complications of pneumonia were over 44 years of age and the eight with recurrence of cystocele were over 40 years of age and had had long duration of symptoms.

Comment

It seems evident that the older the individual and the longer the duration of the pathology, the lower the chance of complete cure. Therefore, cystoceles and rectoceles and the associated pelvic pathology should be anatomically corrected soon after the completion of the family or about 40 years of age, so that the mother can be spared the long years of debilitating symptoms, and have more assurance of complete cure and be better able to assume properly her responsibilities of middle life.

Summary

1. An analysis of 300 cases of anterior and posterior colporrhaphy with associated pathology is presented.

2. From pelvic relaxation to complete prolapse, the process is essentially the same, varying only in degree.

3. Cystoceles and rectoceles are direct traumatic hernias and should be so considered and repaired, with the same meticulous anatomical care as hernias in other locations.

4. The author's steps in the repair of these hernias are presented.

5. A plea is made for anatomical repair of the hernias as soon as the family is completed or when the patient is about 40 years of age.

6. Proper anatomical repair, at about 40 years of age, will prevent long years of disabling symptoms, give more satisfactory results, avoid complications, and enable the mother to have better health to assume her responsibilities in middle life.

References

1. Brentnall, C. P.: J. Obst. & Gynaec. Brit. Emp. **54**: 164-171, 1947.
2. Sears, Nathan P.: AM. J. OBST. & GYNEC. **25**: 484, 1933.
3. Sears, Nathan P.: AM. J. OBST. & GYNEC. **26**: 614-620, 1933.
4. Hill, Howard, and Van Del, D. T.: Surg., Gynec. & Obst. **54**: 108-116, 1932.
5. Davies, Joshua William: Surg., Gynec. & Obst. **54**: 495-504, 1932.
6. Goff, Byron H.: Surg., Gynec. & Obst. **52**: 32-42, 1931.
7. Barrett, Channing W.: Am. J. Obst. & Dis. Women **59**: 553-569, 1909.
8. Cameron, J.: J. Anat. & Physiol. **13**: 438, 1908.
9. Cameron, J.: J. Anat. & Physiol. **13**: 112, 1908.
10. Cameron, J.: J. Anat. & Physiol. **13**: 106, 1908.
11. Barrett, Channing W.: J. Internat. Coll. Surgeons **8**: 242, 1945.
12. Hamilton, John: J. Obst. & Gynaec. Brit. Emp. **50**: 184-188, 1943.

321 WEST BROADWAY

Discussion

DR. E. A. EDWARDS, Chicago.—Dr. Johnson presents a series of 300 patients operated upon for the cure of cystocele, rectocele, and associated uterine diseases. The indications for these procedures are substantiated by the symptoms complained of by these patients. He reviews the accepted operative technics that are used in the repair of these lesions. He suggests an anatomical report of these lesions and makes a plea for their early correction at or before the age of 40.

Certainly we all agree that these patients need an anatomical repair; however, the advisability of their correction at the age of 40 needs some discussion. In this series presented today, 50 per cent of the women were under forty. Repair of these lesions in patients in the child-bearing age, unless adequate sterilization is assured, invites future surgical procedures. These secondary procedures are always much more difficult than the original operations. I believe these lesions should be repaired when symptoms are present and when the family is complete, but that sterilization should be part of the operative procedure.

Many of these lesions do not appear until the patient is sixty or seventy. Then, acutely, a prolapse of the uterus occurs. These extensive cases are more easily repaired than are the smaller lesions. The anatomical planes are more distinctly separable and a more exact anatomical correction is obtained.

It is interesting to observe that in this series, 119 women complained of abnormal bleeding, 112 of a leucorrheal discharge, 24 of postmenopausal bleeding, and 38 of dysmenorrhea in addition to the symptoms attributable to the laceration. We feel that the procedure of choice in patients who have had such symptoms is vaginal hysterectomy and repair. This removes the possibility of future pregnancies, obviates possible future removal of the uterus because of uterine pathology and, above all, corrects most adequately the symptoms complained of. Eighteen patients in this series had cervical amputations and ligations of the Fallopian tubes. We try to avoid cervical amputations unless the amputation is associated with the Manchester operation. Certainly the repair of cystocele, amputation of the cervix, and ligation of the Fallopian tubes is a more trying procedure than to do a vaginal hysterectomy and repair.

A curettage should precede all vaginal operations. Such pathologic lesions as carcinoma of the endometrium and cervix can be diagnosed by this preliminary curettage and investigation and the proper procedure can be instituted.

It should be noted that only three persons in this series had thrombophlebitis. In our fairly large series of vaginal hysterectomy, thrombophlebitis is most unusual and pulmonary embolus has not occurred.

I believe that ten cases of perineal infection in 300 cases is too high an incidence. However, the low incidence of urinary tract infections is exceptional. I would like to ask the author about his management of the postoperative urinary bladder.

It is our policy to correct the lesions as described in this series either by vaginal hysterectomy and repair or by the Manchester operation.

DR. W. O. JOHNSON (Closing).—I wish to thank Dr. Edwards for his frank discussion.

The repairs described are called radical because they entail a complete dissection of the involved parts, a replacement of the organs or structures into their normal positions, and a repair along anatomical lines; complying with the accepted principles of hernial repair of high imbrication of the sac and fascial approximation of the supporting structures.

The cystoceles and rectoceles are direct traumatic herniae, and should be repaired as hernia are repaired. Unless fascial planes are approximated and sutured, the herniae cannot be expected to hold. This procedure is applicable in the young as well as the old and should be carried out before irrecoverable changes occur.

In this series, there were eighteen patients under 30 years of age, where cauterization of the cervix, anterior and posterior colporrhaphy and the Fothergill advancement type of operation were employed. In five of these cases there was a subsequent pregnancy without complications at delivery. Only episiotomies were employed in the deliveries and these patients did not have subsequent pelvic floor relaxations.

In the group of women around 35 years of age, who had completed their family even beyond their financial capacity, an amputation of the cervix, together with vaginal sterilization, and anterior and posterior colporrhaphy was done. Such procedures have restored these women to useful heads of households without premature ovarian failure. There is a relationship between the endometrium and the prolongation of the proper ovarian function, and the above procedures serve both purposes in this group of cases.

The remainder of the cases with cervical amputation were in elderly women with normal uteri for their age, and in every case the uterine cavity was thoroughly curetted to rule out possible pathology. The uteri were left in place to aid in better support, less operative manipulation and risk, and a reduction in morbidity.

We do not advocate a vaginal hysterectomy unless the patient is over 37 years of age, or has intrinsic uterine pathology, fibroids, circulatory changes, etc., which indicates removal of the uterus. An endeavor is always made to suit the indicated operative procedures to the individual case.

Dr. Edwards asked about the postoperative care of the bladder. The postoperative treatment of the bladder in these cases is of greatest importance. The retention catheter which is placed in the bladder at the time of operation is retained for about four days. Continuous drainage is maintained and the bladder irrigated with warm, boric solution daily; once daily 30 c.c. of 5 per cent Argyrol solution is instilled into the bladder. After the fourth day, the catheter is removed and the patient tries to void. If she is unable to void as much as 150 c.c. at a time, a small simple catheter is placed in the bladder in the evening and allowed to drain. This permits rest and reduces bladder edema. In the morning the catheter is removed, and the patient tries to void, and this procedure is repeated until the patient is

completely emptying the bladder. This is determined by catheterizing the patient daily after voiding and (measuring the results) installing 30 c.c. of 5 per cent Argyrol until less than an ounce is obtained by catheter. This procedure avoids later infections in the bladder from residual urine, and affords great comfort to the patient.

It is apparent that the older the patient the longer the duration of the symptoms, the greater the pathology, and the lower the chances for a complete cure. Therefore, cystoceles and rectoceles and their associated pelvic pathology should be anatomically corrected soon after the completion of the family, or about 40 years of age, so that the mother can be spared the long years of debilitating symptoms and be more healthy and better able to assure properly her responsibilities of middle life.

CHANGING CONCEPTS IN CERVICAL BIOPSY*

KENNETH E. COX, M.D., VICTOR B. BUHLER, M.D., AND
WILLIAM C. MIXSON, M.D., KANSAS CITY, MO.

(From the Gynecologic Division of the Tumor and Cancer Service and the Department of Pathology of the Kansas City Municipal Hospital No. 1)

A SERIES of seven cases of equivocal lesions of the cervix are presented. Six of these cases represent all of the lesions in which a problem in diagnosis was encountered by members of the staff in a series of 110 routine biopsies of the cervix performed in a six-month period. Two of these cases are considered to be benign (1 and 2), three intraepithelial carcinoma (3, 4, and 5), one early invasive carcinoma (6), and one both intraepithelial and early invasive carcinoma (7). These diagnoses are not concurred in by all of the members of the staff or by consultants whose opinions were requested.

Warnings as to the possible dangers of erroneous diagnosis of equivocal lesions of the cervix have been sounded before in the literature. TeLinde and Galvin[1] have stated, "The inability of pathologists to diagnose with certainty extremely early lesions has resulted in mistakes of a serious nature. Errors are made in both directions. Benign cancerlike lesions, the result of squamous cell metaplasia and epidermidization, are frequently erroneously called malignant. Early malignant lesions are also not infrequently called benign. Often, when dealing with these cancerlike lesions, the pathologist is in doubt, and he attempts to mask his lack of knowledge by calling them precancerous. This results in unnecessary surgery or irradiation." The failure to realize the relationship of intraepithelial carcinoma to invasive carcinoma, if complete study of the cervix is not attempted in cases where the original biopsy shows only intraepithelial carcinoma, is demonstrated by these authors. Ten cases were reported in which intraepithelial carcinoma of the cervix was treated by removal of the cervix with subsequent finding of definite invasive carcinoma. An eleventh case is reported in which the biopsy specimen showed the only area of invasions, but the removed cervix showed extensive changes in the surface epithelium such as were seen in the biopsies of the other ten cases. In none of these cases was the diagnosis of cancer possible from the palpation or inspection of the cervix.

The seven cases of equivocal lesions presented here were managed as follows:

Case 1.	Benign lesion	Multiple biopsy.
Case 2.	Benign lesion	Scalpel conization.
Case 3.	Intraepithelial carcinoma	Rebiopsy, total hysterectomy.
Case 4.	Intraepithelial carcinoma	Irradiation (radium and deep x-ray).
Case 5.	Intraepithelial carcinoma	Rebiopsy, total hysterectomy.
Case 6.	Invasive carcinoma	Rebiopsy (curette), total hysterectomy, irradiation (deep x-ray only).
Case 7.	Invasive carcinoma	Scalpel conization, irradiation (radium and deep x-ray).

*Read before the Central Association of Obstetricians and Gynecologists on Oct. 24, 1947, in Louisville, Ky.

Although one of these cases of intraepithelial carcinoma (Case 4) was discovered one year prior to the others in this series, two cases (3 and 5), discovered in a total of 110 routine biopsies, represent an incidence of 1.8 per cent. Although the series is admittedly too small to be of statistical value, this high incidence was so surprising to us that we thought comparison of our small series with published reports might be of interest from the standpoint of management of these cases.

Our incidence compares favorably with Schiller's finding of 1.41 per cent "incipient carcinomata" in serial sections of cervices from 425 panhysterectomies,[2] and TeLinde and Galvin's incidence of 1.3 per cent from biopsy material. The incidence of very early invasive carcinoma (2 cases in 110 biopsies) in our series is even higher than the findings of TeLinde and Galvin[1] (2 cases in 240 total hysterectomies).

We felt that our finding of this high incidence of intraepithelial carcinoma and early invasive carcinoma in this series of 110 routine biopsies might be due to the management of most of the cases. We hypothesized that the routine use of rebiopsy and scalpel conization of the cervix with complete microscopic study of the excised tissue, in those cases where an equivocal lesion was present in the original biopsy, might give as complete information as ablation of the cervix or total hysterectomy. That this hypothesis might be correct seemed further substantiated by the findings of Stevenson and Scipiades.[3] In a review of all of the cervical tissue in the files of the Gynecological Pathology Laboratory of the Johns Hopkins Hospital, these authors did not have the patient at hand for additional tissue for study, and their incidence of intraepithelial carcinoma was roughly 0.45 per cent (18 in some 4,000 cases studied).

The incidence of intraepithelial and early invasive carcinoma in our series was roughly comparable to published statistics in routine hysterectomies where the entire cervix was immediately available for study. It was roughly three times the incidence reported in a series where additional tissue was not available for study. These comparisons have led us to believe that if the cervix were available for study in all cases where equivocal lesions are discovered in routine biopsy, a far greater number of intraepithelial and early invasive carcinomata would be discovered than has heretofore been possible.

Conization of the cervix as a diagnostic method in these cases has been considered favorably by TeLinde and Galvin.[1] Combined with low amputation, utilizing the Sturmdorf flap principle, it is the preferred treatment by Martzloff when "carcinomatoid change" is found in the original biopsy.[4] It seems to us that the method of attempting to get a more complete picture of the cervical lesion by scalpel conization might have sufficed as treatment in the two cases in which total hysterectomy was done and no carcinoma, either intraepithelial or invasive, was found in the excised cervix (Cases 3 and 5). In the one case where total hysterectomy revealed early invasive carcinoma (Case 6), scalpel conization would have revealed the lesion, and the cervix and uterus could have been utilized for the local application of radium. Case 4 might either have shown no additional invasive lesion, sparing the patient unnecessary irradiation, or invasive carcinoma might have been found as in Case 7, justifying the irradiation therapy prescribed.

As the result of the study of this small series of cases, we feel that our concepts of cervical biopsy have changed. In the future we will consider biopsy as a screening process in those cervices that present no grossly recognizable cancer. Cauterization of the cervix at the time of the original biopsy will be abandoned so that additional tissue for study will be available if necessary. The finding of equivocal lesions, atypical metaplasia and possible intraepithelial

carcinomata will be followed routinely by a complete sectioning of the original block and wide conization of the cervix. As emphasized by TeLinde and Galvin,[1] the preparation of the tissues will be by the best possible methods, and frozen sections will not be utilized. Conization will be performed with the scalpel rather than the cautery, so as not to desiccate the specimen. A registry of intraepithelial carcinomata of the cervix has been proposed to be sponsored by the local Obstetrical and Gynecological Society. The purpose of this registry will be the confirmation of diagnoses by competent gynecologic histopathologists, and the provision for adequate follow-up of these cases.

It is felt that in the study of a lesion in which the highest order of opinion with respect to its true nature is still divided, concerted action by a group of gynecologists and pathologists will progress faster than individuals working alone.

CASE 1.—Aged 18 years, para 0, gravida i. Irregular vaginal bleeding three and one-half months. Never any cramps.

Uterus enlarged the size of a three and one-half months' pregnancy, cervix markedly hypertrophied, large raised circumoral erosion hyperemic and covered with mucopurulent exudate and bled easily to touch in all areas.

Biopsy report: "Cervical granuloma showing decidual reaction with acute and chronic inflammation" (Fig. 1).

Consultant (pathologist) unwilling to state that epithelial lesion was not carcinoma. Another biopsy recommended.

New biopsy performed, a total of five times in a period of four weeks. All sections showed metaplasia with decidual reaction and a disappearance of the inflammatory reaction following penicillin therapy. The cervix was not cauterized, pregnancy continued to normal term delivery, at which time cervical biopsy disclosed decidual reaction.

CASE 2.—Aged 19 years, para i, gravida ii. Curettage for continued bleeding following spontaneous abortion at two and one-half months. Cervix showed no gross lesion.

Diagnosis of material removed with dull curet: "Chronic cystic endocervicitis with squamous cell metaplasia." Rebiopsy requested.

Six weeks following original curettement and because of the equivocal nature of the marked metaplasia seen in the original curettement, scalpel conization performed. Cervix showed no gross lesion.

Biopsy report: "Cervix showing squamous cell metaplasia" (Fig. 2).

CASE 3.—Aged 23 years, para iv, gravida iv. Abdominal pain intermittent for two years, worse for one month. Profuse leucorrhea for several years. No metrorrhagia. Last menstrual period three weeks prior to biopsy.

Uterus anterior and normal size, bilateral adnexal tenderness. Cervix was the site of an extensive circumoral erosion which bled in all areas.

Biopsy report: "Chronic cervicitis with squamous cell metaplasia."

Because of the extensive nature of the erosion and its vascularity, rebiopsy done three days later and adjacent to the previous biopsy.

Biopsy report: "Intraepithelia carcinoma" (Figs. 3*A* and 3*B*). Consultant (pathologist) agreed.

Total hysterectomy with conservation of both tubes and ovaries. Histological section of multiple blocks of the excised cervix failed to reveal any additional foci of intraepithelial carcinoma or invasive carcinoma.

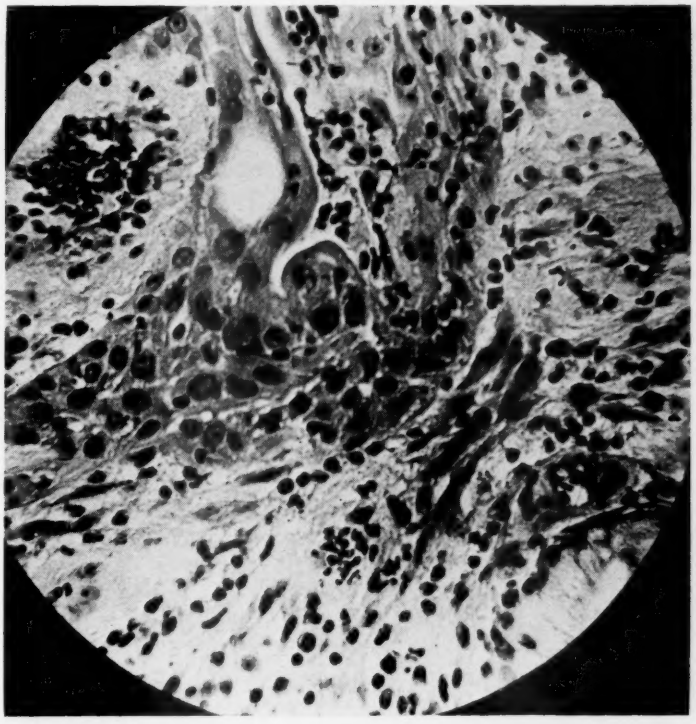


Fig. 1.—High power view of group of cells extending into underlying stroma. Delineation is well established and little variation in staining properties apparent. (×215.)

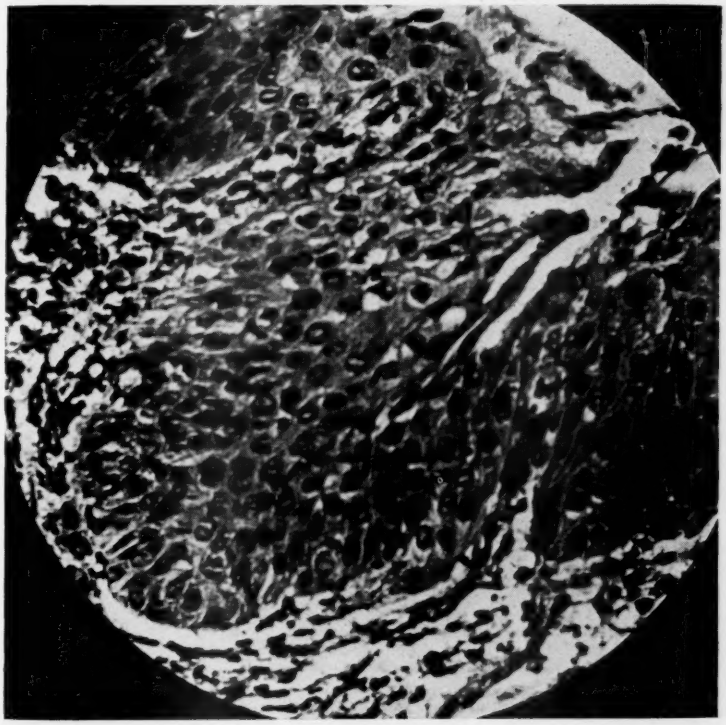


Fig. 2.—Portion of lining of endocervix removed at scalpel conization. This benign lesion shows uniformity of size and staining properties of the metaplastic cells. (×215.)

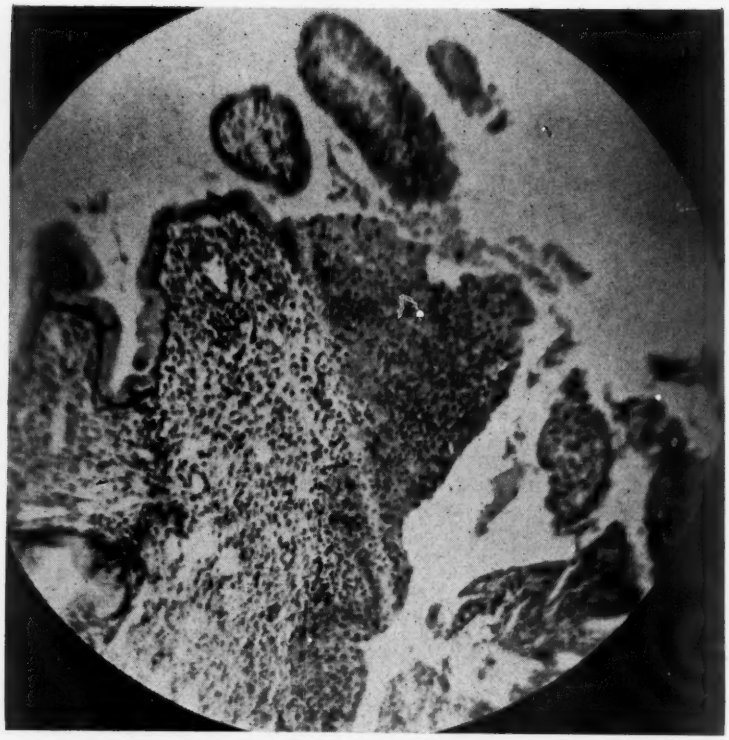


Fig. 3*A*.—Rebiopsy three days later showing blending of normal endocervical lining with full thickness of atypical cells. (×50.)

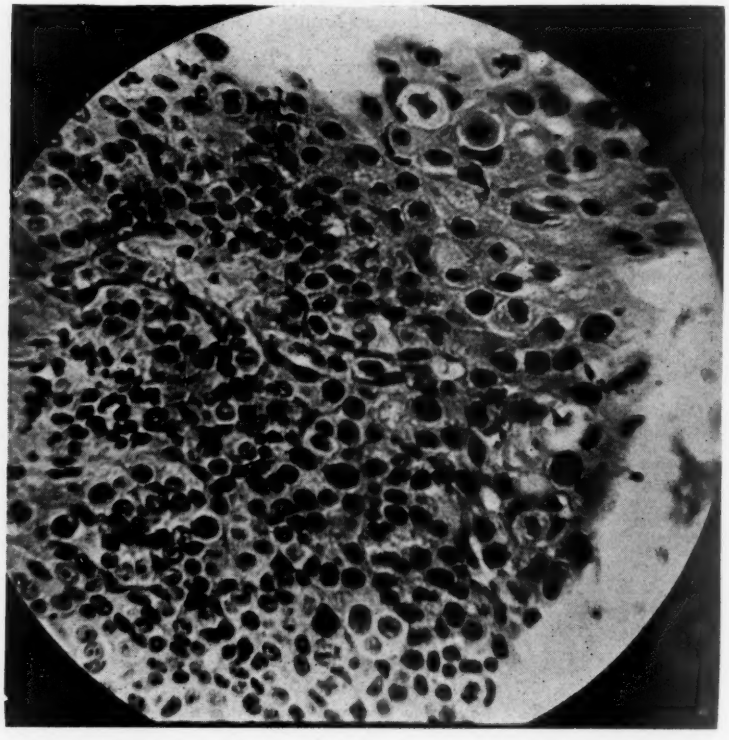


Fig. 3*B*.—Marked variations in size, shape, and staining property of cells. Mitoses are common. (×215.)

CASE 4.—Aged 53 years, para vii. Menopause two years previously, no bleeding since.

Small endocervical polyp with small area of erosion at the margin of the external os which bled easily on touch. Uterus normal size in third degree retroversion.

Polyp removed and vascular area biopsied. Cervical polyp was benign.

Cervical biopsy report: "Squamous cell metaplasia, carcinoma in situ" (Fig. 4). Slide was submitted to two pathologists in consultation. One diagnosed carcinoma of the cervix; the second, carcinoma in situ.

Subcervical and tandem application of radium for a total of 6,600 mg. hours was followed by deep x-ray therapy.

CASE 5.—Aged 38 years, para ii, gravida ii. Interval bleeding for one year.

Normal pelvic organs except for typical circumoral "erosion." Biopsy taken from the only area in erosion which bled on touch.

Biopsy report: "Diagnosis deferred. Equivocal lesion of the cervix. More tissue requested."

Biopsy of the cervix nine days after the original biopsy. Report: "Carcinoma in situ of cervix" (Figs. 5*A* and 5*B*).

Total hysterectomy, bilateral salpingectomy and oophorectomy. Dense pelvic adhesions of tubes and ovaries were found at operation.

Multiple sections of excised cervix showed *no carcinoma* in situ.

CASE 6.—Aged 31 years, para o, gravida i. Menometrorrhagia one year. Last menstrual period three weeks previously. Previous bilateral salpingectomy.

Cervix negative in appearance with pin-point os. Uterus 180 degree anteflexed with fundus enlarged symmetrically twice normal size. Uterine cavity could not be entered due to the marked anteflexion. Endocervix was curetted.

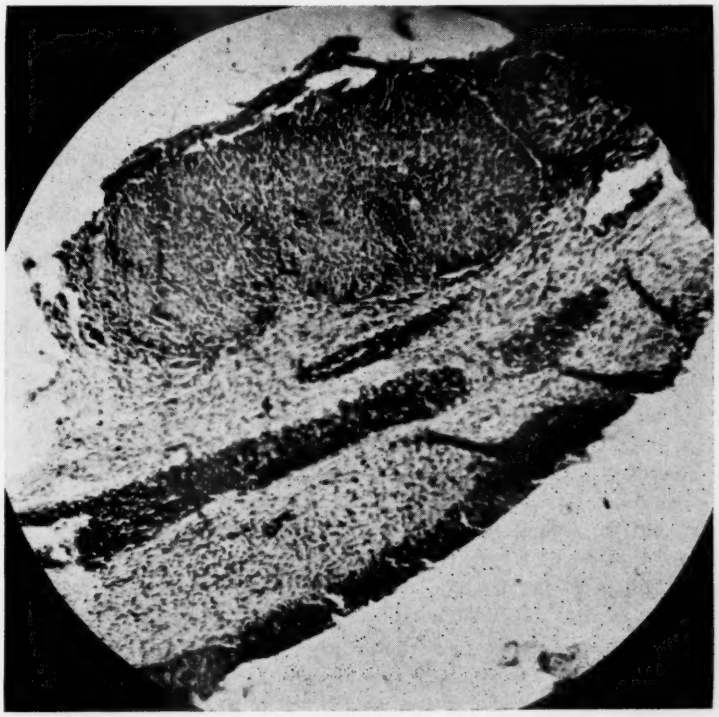


Fig. 4.—Single nest of atypical cells in the endocervix. Membrane prominent with no evidence of invasion. (×50.)

Diagnosis: "Endocervix showing squamous cell metaplasia." Slide reviewed four weeks later at request of resident pathologist. Diagnosis amended: "Squamous cell carcinoma of the cervix, Grade II."

Consultant (pathologist) disagreed. Diagnosis: "Metaplasia."

Endocervix again curetted three days later. Diagnosis: "Cervix showing squamous cell metaplasia."

Total hysterectomy and right oophorectomy performed, left ovary conserved. Original section of excised cervix showed only metaplasia (Fig. 6*A*). Cervix recut and section reported: "Squamous cell carcinoma, Grade 2" (Fig. 6*B*). Following the establishment of the diagnosis of invasive carcinoma of the cervix, deep x-ray therapy was instituted.

CASE 7.—Aged 42 years, para ix. Menorrhagia three months. Cervix showed elevated avascular area at the margin of the external os subsequently shown to be a deep retention cyst. An applicator introduced into the cervical canal was blood tinged. Remainder of pelvic organs normal. Curettement of endocervix performed.

Biopsy report: (Endocervical curettings.) "Squamous cell carcinoma of the cervix" (Fig. 7*A*). Further tissue requested to differentiate between intraepithelial and invasive carcinoma. Scalpel conization performed. Original section showed intraepithelial carcinoma (Fig. 7*B*). Recut of block showed definite invasive carcinoma.

We wish to thank Dr. Ferdinand C. Helwig for the help and advice he has given us in the preparation of this paper.

References

1. TeLinde, R. W., and Galvin, G.: AM. J. OBST. & GYNEC. **48**: 774-797 (Dec.), 1944.
2. Schiller, W.: Surg., Gynec. & Obst. **56**: 210-222 (Feb.), 1933.
3. Stevenson, C. S., and Scipiades, E.: Surg., Gynec. & Obst. **66**: 822-835 (May), 1938.
4. Martzloff, K. H.: AM. J. OBST. & GYNEC. **48**: 774-797 (Dec.), 1944.

Discussion

DR. HERBERT E. SCHMITZ, Chicago.—The presentation of Drs. Cox, Buhler, and Mixson is timely and should serve as a stimulus to the members of this society to emulate their procedure. We have for years proposed routine biopsy of all cervical lesions irrespective of their clinical appearance, claiming that the microscope was the only adequate method of diagnosing early cancer. A biopsy forceps and bottle of fixative should be found on every gynecologist's instrument table next to the vaginal speculum. Just what changes we may interpret as cancer are still debatable and some of us choose to err on the radical side rather than to sacrifice a life by our attempt to be ultraconservative. If doubt exists, repeat biopsy, conization, amputation of the cervix or vaginal hysterectomy with conservation of the ovaries is indicated.

Cases 1 and 2 in this series demonstrate the great difficulty in properly interpreting lesions occurring in the cervix during pregnancy. Further studies of the cervical changes occurring during pregnancy are needed. In Cases 3 and 4 the diagnosis seems quite evident, and total hysterectomy with conservation of the ovary in the younger woman the method of choice. In Case 4 either removal of the uterus and the adnexa or irradiation would suffice. The same would hold for Case 5. Cases 6 and 7 illustrate the need of careful recheck of all doubtful cases so that incomplete treatment is not carried out. A registry such as the essayists advocate will be of great value in giving others an opportunity to review questionable microscopic sections and thus improve their own diagnostic ability.

Early diagnosis of cervical cancer offers the greatest weapon in the successful treatment of this condition. Through lay education we are seeing the patient at a time when careful examination of the genital tract is necessary. If we overlook a serious lesion and reassure our patient falsely we send her to her doom. May I again appeal to the members of this society to follow in the footsteps of Dr. Cox and his co-workers.

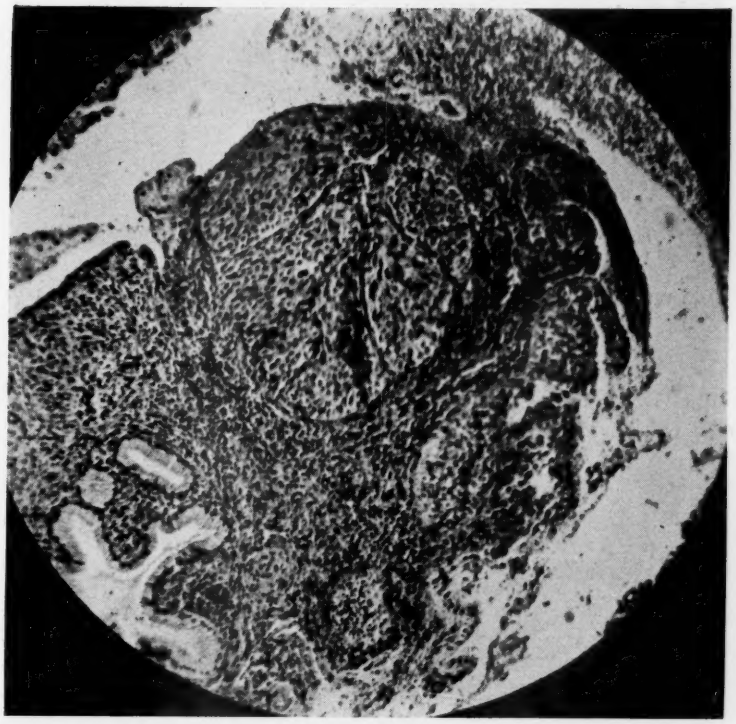


Fig. 5*A*.—Area of intraepithelial carcinoma. Note well defined basement membrane. (×50.)

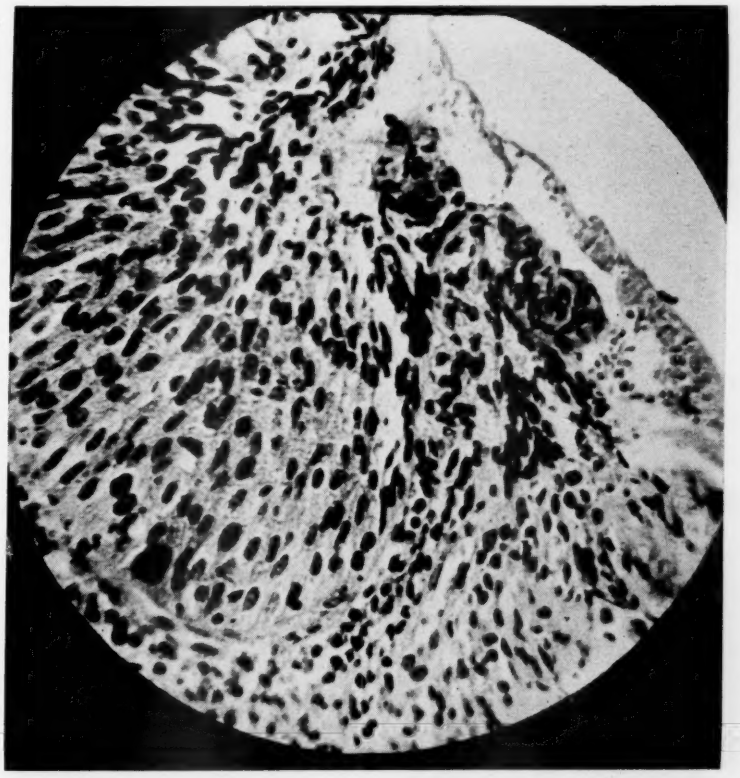


Fig. 5*B*.—High power magnification to show cell type. (×215.)

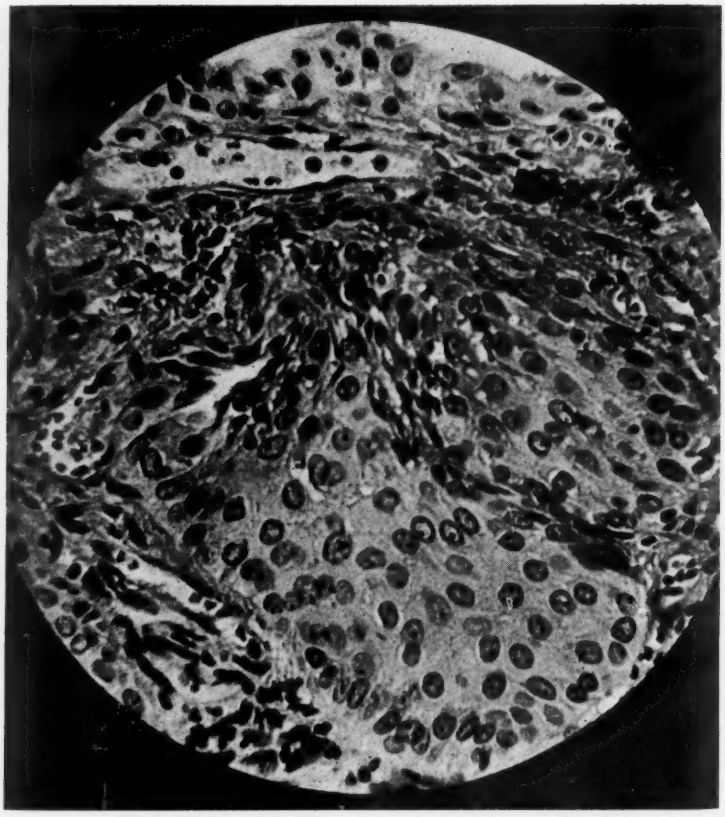


Fig. 6*A*.—Area of squamous cell metaplasia noted in first block of tissue from cervix removed at panhysterectomy. Lesion considered benign. (×215.)

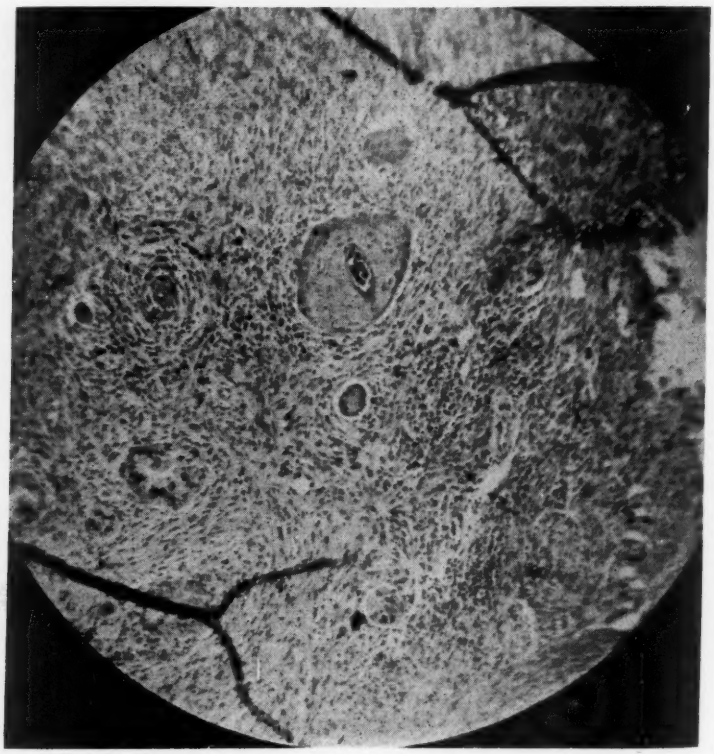


Fig. 6*B*.—Section taken from further block cut from cervix removed showing definite invasive carcinoma. (×50.)

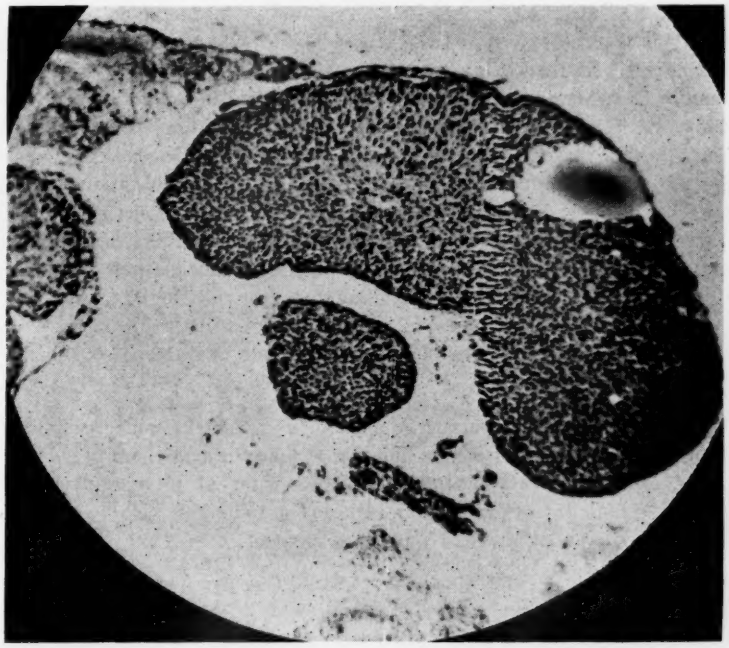


Fig. 7*A*.—Tissue removed at curettement of internal os. Definite neoplastic nature of the cells established. Absence of supporting tissue makes differentiation between intraepithelial and invasive carcinoma impossible. (×50.)

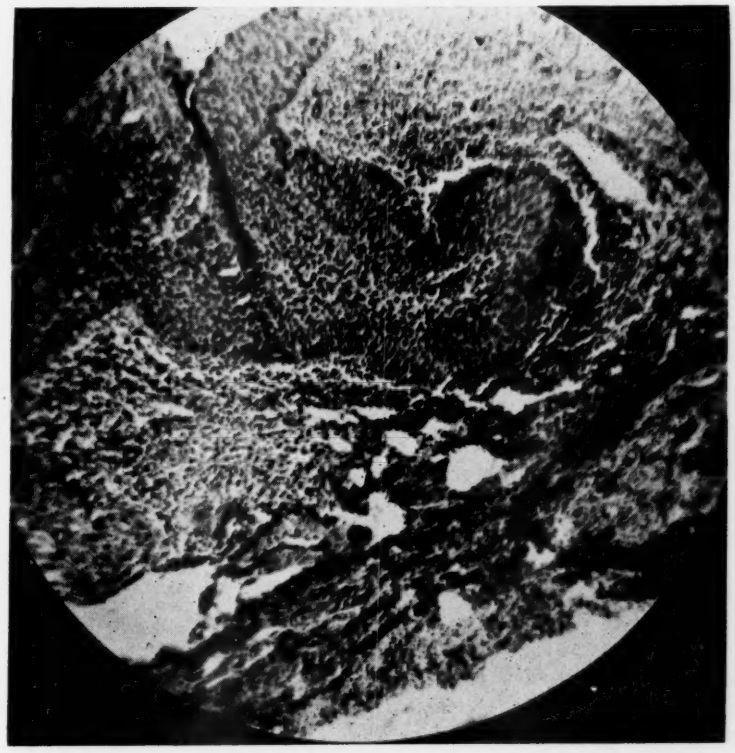


Fig. 7*B*.—Nest of well delineated neoplastic cells demonstrated in the first section taken from tissue removed by scalpel conization. (×50.)

DR. JOHN HUFFMAN, Chicago.—Dr. Arthur Curtis has long emphasized that the diagnostic removal of a piece of tissue from the cervix for the diagnosis of early cancer is not the procedure of choice. Instead, wide removal of all unhealthy tissue from a suspicious cervix is to be preferred. If necessary the unhealthy cervix should be amputated. Such an amputation will not only obtain sufficient material for adequate study but will remove diseased tissue which would have been a potential danger in the future. Needless to say, when a suspicion of malignancy has been raised, many blocks should be taken and many sections cut from each block. Dr. Cox's report has emphasized the necessity for adequate training at our teaching centers of young men in gynecologic pathology. It is an indispensable part of the residential training of the gynecologist and until we have adequate pathological material for our residents and junior staff we will not produce competent gynecologists. We have all had the experience of equivocal reports from general pathologists. Until we cut our own "blocks" and, until we train our young men to interpret adequately their own tissue specimens, we will continue to have difficulties.

DR. COX (closing).—I appreciate Dr. Schmitz's remarks concerning vaginal smears. We did not mention these because we do not know much about them. The problem of the diagnosis in these extremely early lesions is still a matter of interpretation of cancer cells in the tissue itself, requiring training and experience to enable one to diagnose such cells when isolated on a smear, and that is beyond us at present.

VAGINITIS EMPHYSEMATOSA*

HERMAN L. GARDNER, M.D., HOUSTON, TEXAS

(From the Department of Gynecology, Baylor University College of Medicine, and the Texas Medical Center)

OF SUCH rarity is the condition variously known as vaginitis emphysematosa, colpohyperplasia cystica, and emphysematous colpitis, that it might well be placed within the realm of medical curiosities.

After encountering the condition and being totally ignorant of its nature, its characteristics were discussed with some forty obstetricians and gynecologists. None of these recalled having seen anything similar and only one expressed any knowledge of such a lesion. An assumption could then be made that the condition is comparatively unknown.

The lesion was first described by Hugier[1] in 1847 and subsequently by several German authors. The German literature of the nineteenth century contains a relatively large number of case reports. The combined literature of America and Great Britain contains the reports of only eleven authentic cases[2-9] of vaginitis emphysematosa. Four other cases[10, 11] might be included, but from the descriptions given there seems to be little similarity. Since the history of the lesion was well covered by Ingraham and Hall[4] in 1934, further historical data will be omitted.

The characteristic lesion is one of gas-filled cystoid cavities of the mucosa and submucosa of the vagina and cervix. The lesion usually involves both the upper vagina and the cervix, but occasionally is limited to one site or the other. Vaginitis emphysematosa is more often seen during pregnancy. The condition is productive of only mild, if any, symptoms. The point of greatest interest concerns its etiology and this remains obscure. Although several theories have been formulated as to its development, none seem acceptable to our present-day pathologists with their increased knowledge of causes and pathogenesis of diseases.

Case Report

Mrs. M. C., white, aged 32 years, gravida iv, para ii, came under observation as a private patient on Aug. 19, 1946, at which time she was pregnant, being twelve weeks past her last mentrual period. She presented no symptoms except those of early pregnancy and her general physical examination showed nothing unusual. Blood examination showed red cell count 3,110,000; hemoglobin 8.2 Gm.; white count 8,900 with neutrophiles 70, leucocytes 29, eosinophiles 1; Kline and Kahn tests negative; Rh factor positive; sedimentation rate (Wintrobe) 17 mm. The urine was negative for sugar and albumin. Pelvic examination showed moderate relaxation of all pelvic supports; the uterus corresponded in size to that of a twelve-week pregnancy.

The lesion with which this presentation is concerned appeared on the cervix. The cervix was softer than the usual cervix in pregnancy, to the extent that it was difficult to outline by palpation. Speculum examination showed the cervix to have a bulk four or five times that of normal. This enlarged cervix was filled with, or almost replaced by, opalescent lesions resembling Nabothian cysts. The cysts were limited to the cervix and they varied in diameter from one to fifteen millimeters. When the cervix was wiped briskly with a cotton tipped

*Read before the Central Association of Obstetricians and Gynecologists on Oct. 24, 1947, in Louisville, Ky.

applicator a sound was elicited much like that produced when a small rubber balloon is pinched between the fingers. It was immediately evident that the cystoid spaces contained a gas rather than the usual mucus of nabothian cysts. Some of the larger lesions were punctured with a sharp-pointed scalpel and only gas escaped, there being no exudate nor secretion of any type. The gas-filled spaces were discrete and independent, each failing to lose its gas, and thus its contour, when neighboring cavities were punctured. That these spaces had no communication with each other was further shown by minute examination of excised wedges of the cervix subsequently removed. Firm palpation produced no crepitation as would be expected in true emphysema. The gas-filled cavities projected slightly above the general contour of the cervix. The epithelium covering the larger vesicles was thin and translucent. The lesions were so numerous that only patches of normal appearing cervical mucosa were present. The mucosa of the vagina was normal and there was no unusual discharge.

Repeated wet smear examinations of the vaginal secretions showed no trichomonads. Repeated vaginal smears stained by Gram's method showed gram-negative cocci predominating. No *Monilia albicans* nor other type of fungus was seen on stained smears, and there was no growth on Sabouraud's. The vaginal secretions tested with nitrazine paper showed a pH of about 7. Bacterial cultures were made by incising the epithelium over the cystoid spaces and swabbing their interior with cotton tipped applicators. Plants on the following media showed no growth: brain heart infusion blood agar, aerobic and anaerobic; glucose heart infusion semisolid agar deeps; anaerobic agar (BBL); brain heart infusion broth and Sabouraud's.

Washings were obtained from the cystoid lesions by injecting and aspirating normal saline through a hypodermic needle. These washings (0.5 c.c.) were injected into the vaginal wall of a mature rabbit. Gross and microscopic examinations of the vaginal wall after seven days showed no evidence of gaseous lesions. Since a rabbit's vagina is not necessarily susceptible to the same diseases as a woman's vagina the test may bear no significance.

At seventeen weeks' gestation, with the patient under cyclopropane anesthesia, a generous wedge of tissue was removed from the cervix for pathologic study. The patient was frequently examined throughout her pregnancy but no marked changes in the cervix were discernible. At thirty eight weeks' gestation the patient developed a premature separation of the placenta with an estimated blood loss of 300 c.c. Labor ensued immediately. After three hours, spontaneous delivery of a normal six pound, two ounce male infant occurred.

Palpation and close inspection of the cervix following delivery showed clearly that the gaseous lesions were limited to the portio vaginalis. There was no evidence that any of the cystoid spaces had ruptured during labor and there were no lacerations. After delivery of the placenta two large wedges of cervix were excised (Fig. 1). Upon removal of these wedges of tissue it was apparent that the entire thickness of the cervix was involved, the organ being literally honeycombed with the gas-filled lesions. When these pieces of tissue were submerged in water they were noted to bob to the top with the rapidity of a fishing cork. When a cavity was punctured beneath water, bubbles of gas would escape and rise to the surface.

The patient's puerperium was entirely uneventful. Examination of the cervix on the fifth postpartum day showed many of the lesions present, but their size had markedly diminished. Examination of the patient on the fourteenth postpartum day showed only three or four small lesions remaining. These were on the posterior lip at the site of some previously very large cysts. Examination six weeks postpartum showed a cervix essentially normal, free from cysts of any kind and with no erosion.

Microscopic Findings

(Tissue taken at 17 weeks' gestation.) Sections of cervix reveal surface covered by mature stratified squamous epithelium with slight parakeratosis. The fibromuscular tissue contains in places numerous inflammatory cells, chiefly lymphocytes with occasional polymorphonuclear eosinophiles and polymorphonuclear neutrophiles. A few macrophages

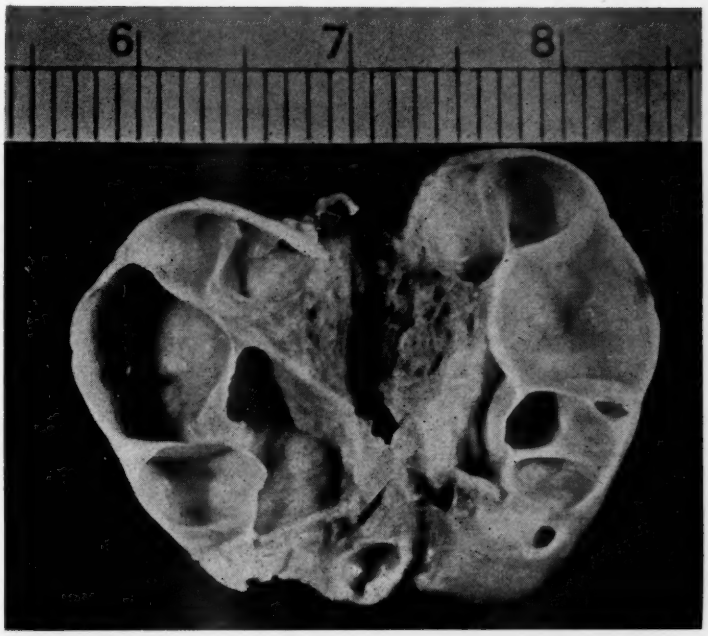


Fig. 1.— Gross appearance of cervical tissue removed at time of delivery. Incised and spread open. The centimeter rule indicates size of individual gas-filled cystoid locules.

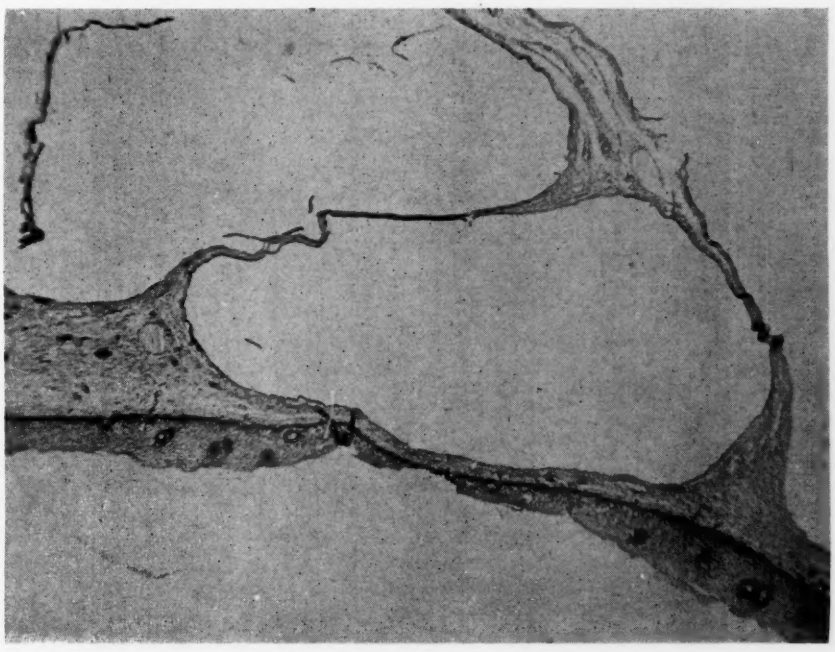


Fig. 2.—Only thin partition separating some gas-filled cavities (×15).

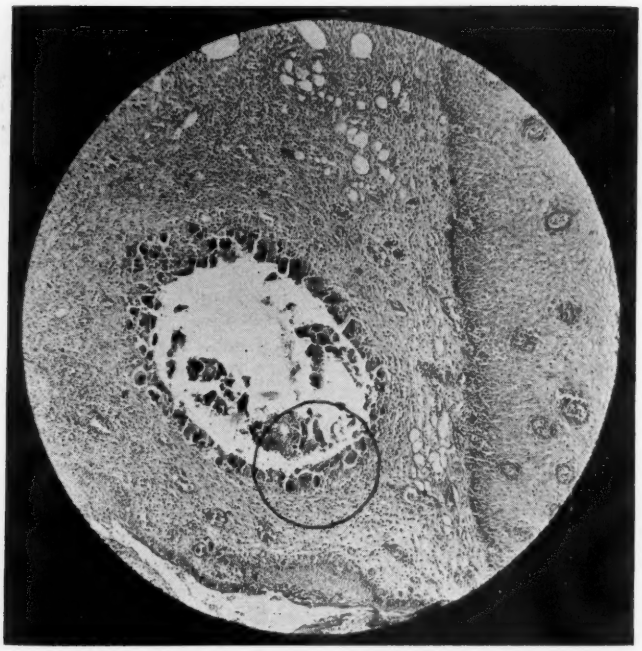


Fig. 3.—Low power of a very small gas-filled cavity lined with large undistorted multinucleated giant cells (×65).

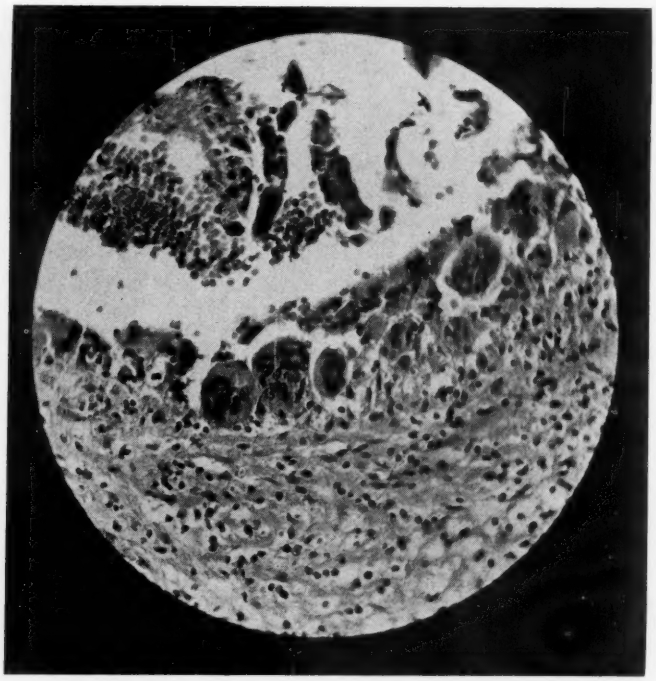


Fig. 4.—High power from encircled area in Fig. 3. Giant cells are clearly shown. The red blood cells within the lumen are presumed to have resulted from trauma at the time of removal. Some giant cells have been shed into the lumen (×250).

are present and contain blood pigment. The most striking finding is the presence of giant cells and cysts. The cysts vary in size from small microscopic structures to large ones where only a part of the wall can be included in a low-power field. The cysts appear to be empty. Lining these cysts are numerous giant cells, some of which project as oval or rounded multinucleated cells giving an irregular lining. These cells usually contain six to twelve nuclei which are round or oval. The cytoplasm is stained pink by eosin and is finely granular, nonvacuolated, and contains no demonstrable organisms. In part these cells are flattened as if compressed by pressure and have a syncytial appearance. Multinucleated giant cells are not confined to the immediate cyst wall but extend a short distance into the adjacent fibromuscular tissue of the cervix. A few clusters of these multinucleated giant cells of larger sizes are seen in inflammatory areas without cyst formation surrounded by numerous inflammatory cells, chiefly lymphocytes. In the immediate vicinity of the giant cells the tissues are loose, and numerous small spaces are formed by strands of loosely arranged tissue, and the impression is given that these are the early stages of cyst formation. No semblance of definite cyst wall has yet formed here. Occasional cysts near the surface are in part lined by mature stratified squamous epithelium. The blood vessels and lymphatics in these sections are prominent. A few are lined by swollen endothelium.

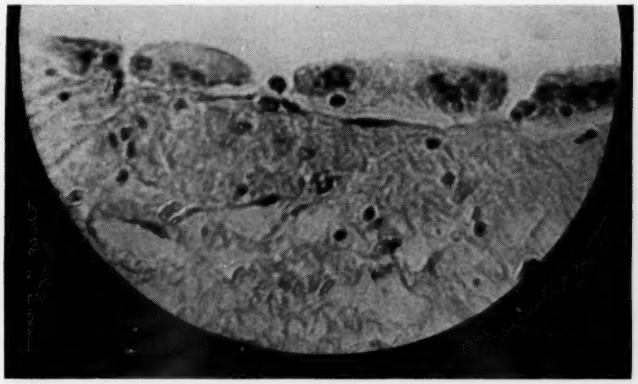


Fig. 5.—High power of a larger lesion showing giant cells partially flattened from intracystic pressure. Giant cells in most lesions are more compressed (×400).

Cervical tissue removed at time of delivery reveals on microscopic examination the following: Mild focal chronic inflammatory reaction and cysts. The inflammatory reaction consists principally of lymphocytes. The cysts are much larger than those seen in previous biopsy specimen. The very large cysts frequently lack specialized cells and appear to be lined by stretched out cervical stroma. In a few places are seen very thin syncytial type cells suggesting greatly compressed giant cells. A few less large cysts near the surface possess an almost intact syncytial type lining. There are present a few definite multinucleated giant cells, only moderately compressed and flattened. These, too, form part of the cyst lining. Some cysts are close together and have a thin common wall separating the cysts. The fibromuscular cervical tissue is loose and edematous. Moderately prominent blood vessels and lymphatic vessels are noted. Surface stratified squamous epithelium appears vacuolated and intercellular bridges are more prominent than usual. Gram's stain reveals no organisms. Fat stains reveal little fat present, there being none in the cystic cavity. A few giant cells contain multiple small droplets of well-stained fat but the vast majority contain no stainable fat.

Discussion

Neither the origin nor the chemistry of the gas contained within the cystoid spaces has been determined. Ingraham and Hall[4] have given a complete review of the literature and they have described their attempts at

determining the nature of the gas. They have shown that the gas is not pure oxygen, carbon dioxide, trimethylamine, nor hydrogen sulfide. Their work has indicated, and the assumption of others has been, that the gas could be air, but the volume of gas available has always been too small for accurate analysis.

I should like to present arguments opposing the idea that the gas is air. That air could be present in the vaginal canal under sufficient pressure to be forced into the cervical and vaginal tissues seems only remotely possible. Instead of having a true emphysema with a free movement of gas within the tissue spaces, with a characteristic crepitation on palpation, we have what appears to be totally independent gas-filled locules from which the gas is not displaceable. Since it is probable that there is a constant absorption into the blood stream of any gas within living tissues, it should be assumed that a continuous and endogenous source of gas does exist. If all evidence is correct that these numerous locules are discrete, the necessity would then be that each cavity must have its own source of gas for its maintenance, or for its increase in size as individual locules can be observed to do during an extended period of observation.

A more rational view would seem to be that the gas is other than air and that it has its origin within the tissues. Whether we are dealing with a rare form of degeneration or decomposition, a slow-growing, gas-forming microbe or some other unknown process, is a point obviously unsettled. Although the bacteriologist reported no growth on various aerobic and anerobic culture media, and careful bacteriological investigation by others has failed to prove a bacterial cause, the idea should not be totally discarded. Slow-growing bacteria, offering difficult cultural problems, such as acid-fast bacilli frequently produce giant cells, and it is possible there is one capable of producing gas.

Concerning the giant cells partially lining many of the cystoid cavities, several authors have made the assumption that they have resulted from the gas acting as a foreign body. This view may be entirely correct but it does not fully explain the giant cells in the stroma outside of and away from gaseous cavities as appear in the case presented. That isolated groups of giant cells (Fig. 6) do exist would seem to indicate that they have not resulted from the gas acting as a foreign body, but rather that the gas and giant cells are elements of the same endogenous process.

Some possible stages in the development of this lesion are shown diagrammatically in Fig. 7. This idea was conceived by the author after much study of the microscopic sections.

Lesions similar, and probably analogous to vaginitis emphysematosa are cystitis emphysematosa of the urinary bladder and pneumatosis cystoides intestinalis. Since these lesions of unknown etiology affecting the urinary bladder and intestinal tract resemble vaginitis emphysematosa in so many respects, a logical assumption would be that the three have a related etiology.

Summary and Conclusion

1. A rare and interesting lesion has been called to the attention of the members of this society and a case report is being placed on record.

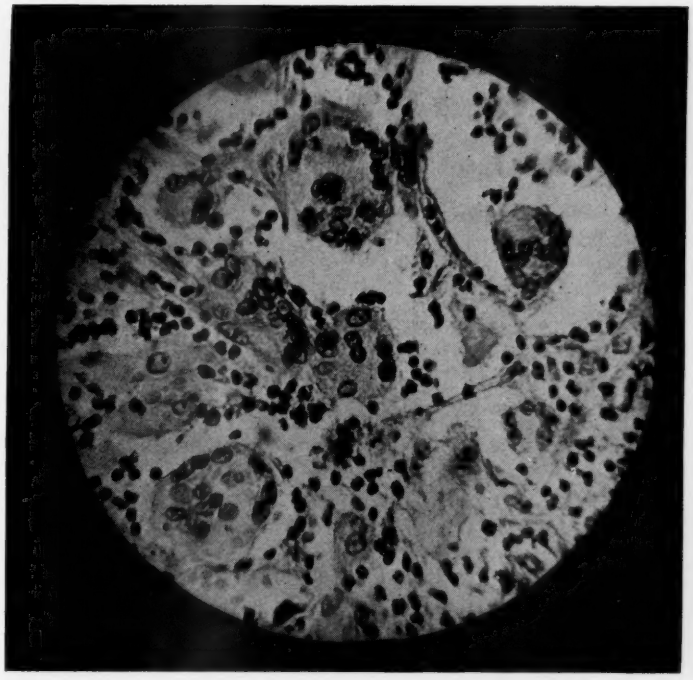


Fig. 6.—Isolated group of giant cells away from gas-filled cavity. Note loosely arranged stromal tissues. This possibly early stage of gas-filled cystoid lesion (×400).

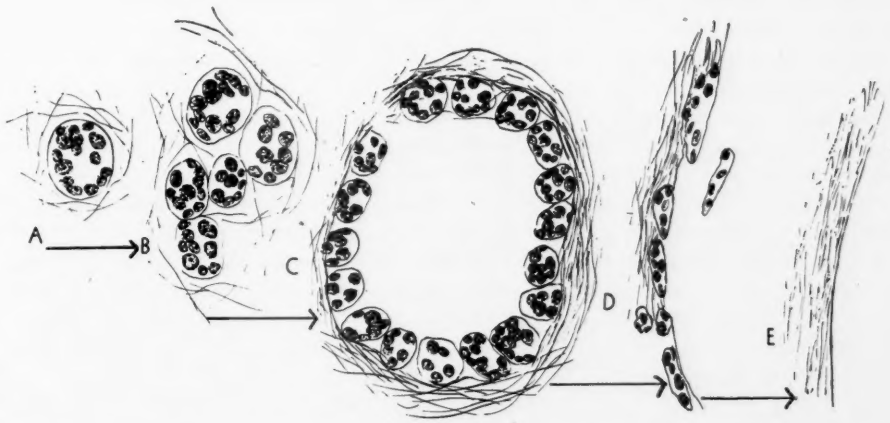


Fig. 7.—Some possible stages in pathogenesis: *A*, Giant cell. *B*, Group of giant cells. *C*, Small gas-filled cystoid lesion lined with large undistorted giant cells. *D*, Larger cystoid lesion with lining giant cells partially flattened from intracystic pressure. Occasional giant cell detached. *E*, Largest lesions lined chiefly with stretched out cervical stroma, presumably the majority of the giant cells having been shed into the lumen, although an occasional very thin giant cell can usually be seen in the largest lesions.

2. It is probable that the lesion is a pathologic entity but without great clinical significance.

3. The etiology of the lesion remains obscure.

4. There is little evidence that the lesion is productive of symptoms.

5. Argument is presented supporting an opinion that the gas within the lesions has an endogenous origin as opposed to an assumption that the gas is air.

6. Some possible stages in pathogenesis have been suggested.

The author expresses his sincere appreciation to Dr. Stuart A. Wallace, Department of Pathology, for the microscopic descriptions, and to Dr. Preston E. Harrison, Department of Bacteriology, for the bacteriological studies.

References

1. Hugier: Bull. et mém. Soc. de chir. de Paris **1**, 1847.
2. Jackson, J. M., and Wright, J. H.: Boston M. & S. J. **139**: 82, 1898.
3. Heaney, N. S.: Am. J. Obst. & Gynec. **15**: 256, 1928.
4. Ingraham, C. B., and Hall, I. C.: Am. J. Obst. & Gynec. **28**: 772, 1934.
5. Marshall, C. J., and Bergstrom, V. W.: Am. J. Obst. & Gynec. **29**: 282, 1935.
6. Robberson, J. H., and Owen, May: Am. J. Obst. & Gynec. **32**: 1062, 1936.
7. Buxton, B. H.: Tr. New England Obst. & Gynec. Soc. May 14, 1941.
8. Gervis: Obst. Trans. Vol. XXVI: 144, 1884.
9. Herman, G. E.: Lancet **1**: 1252, 1891.
10. Wright, H. E.: Lancet **2**: 87, 1892.
11. Oliver, James: Brit. M. J. **2**: 805, 1894.

Discussion

DR. CLARENCE INGRAHAM, Denver, Colo.—This is a most interesting and unusual condition. This patient mentioned a feeling of fullness and had been conscious at times of the rupture or bursting of a cyst, producing an audible noise, but being practically devoid of symptoms. As Dr. Gardner has said, the main interest lies in the determination of the method of formation of these cystoid cavities.

There are two similar lesions, analogous in some respects, occurring elsewhere in the body. With pneumatosis cystoides intestinalis, in this affection, gas-filled vesicles appear in the wall of the intestine, chiefly beneath the serosa of the ileum, but also of the colon. The other lesion, cystitis emphysematosa, described by Mills and others, shows vesicle formation in the bladder wall.

The same discussion arises concerning the etiology of these gas-filled vesicles as in emphysematous vaginitis. Is the gas derived from bacteria, or is air forced into the tissues through minute lesions by mechanical pressure?

I have had the opportunity of observing three cases of emphysematous vaginitis which occurred in the Colorado General Hospital, two were in pregnant women, the third in a patient from the Psycopathic Hospital, who died from strangulation with food and was autopsied eight hours later. This patient had a thin-walled hydrosalpinx on the right, the left tube was closed and thickened, the ovaries and uterus were grossly and microscopically normal. The vagina was studded with small cysts 1 to 3 mm. in diameter, many had broken down and coalesced to form small ulcers. The cysts contained gas under pressure and were microscopically similar to the two cases in the pregnant women. Cultures taken from the cysts remained sterile for three days, but on the fourth an aerobic spore bearing nongas-forming rod developed which we interpreted as an accidental contamination. There were no bacteria in the microscopic stained specimens made from the walls of the cysts.

In the two pregnant women, extensive examinations were carried out by Dr. Ivan C. Hall who was then head of the bacteriological department of the Colorado School of Medicine, and who is coauthor of the paper on emphysematous vaginitis, which we published in The American Journal of Obstetrics and Gynecology, November, 1934.

Microscopic and cultural examinations were made from the vaginal fluids using the various media and staining materials. Nothing out of the ordinary was obtained except that in our first case a gram-negative vibrio was repeatedly and abundantly seen, but could not be cultivated. Cultural examinations were made of the gaseous cysts. The results were negative in all but one instance when an unidentified nongas-forming rod was recovered. These findings were interpreted as an indication that the cysts were actually sterile.

Several injections of vaginal fluid of both pure and mixed cultures and from the cysts' contents were made into the vaginal wall of rabbits and guinea pigs. In several instances there were marked inflammatory changes, with abscess production in one instance, but no lesions suggestive of emphysematous vaginitis.

The lesion being a harmless affection, on two occasions with permission, the vaginas of pregnant women were swabbed with the secretion from one of our patients, but nothing resulted.

The blood serum of one patient was tested for agglutinins with each of the bacterial strains recovered from the cultures. The results were negative excepting with Döderleins lactobacillus.

Efforts were made on two occasions to determine the character of the gas—14.5 c.c. was aspirated into a syringe, the plunger anointed with petrolatum jelly and the gas aspirated from the base of the cysts. All tests were conducted in the syringe at 24° C., by emersion in water at that temperature. Sulphnine acid 5 per cent was first drawn into the syringe and shaken for fifteen minutes with the needle submerged. There was no reduction in volume, which was interpreted as a failure to demonstrate trimethylamine, a gas claimed by Zweifel and early investigators as present. This gas has a fishy odor and occurs in the vaginas of pregnant and nonpregnant women. The acid was washed out with water and replaced with 1.7 normal sodium hydroxide and also shaken with the gas for 15 minutes. Again there was no absorption excluding carbon dioxide.

Saturated pyrogallic acid was drawn into the syringe and mixed with sodium hydroxide. The surface of the liquid in the syringe became dark and during two hours' contact, with frequent shaking there was a reduction of about 21 per cent in volume, suggesting oxygen. The remainder was tested for inflammability with negative result. If it were nitrogen the composition of the gas would seem to be practically identical with that of air. These experiments were carried out by Dr. Robert Hill of the biochemical department of the University.

In order to investigate the persistance and reaction produced by gas in the tissues, experimental subcutaneous emphysema was produced by injecting air subcutaneously in a rabbit. Five days later the rabbit was killed. Postmortem examination showed scattered patches of small gas-containing vesicles in loose ariola tissue with no gross evidence of inflammation. Sections of the tissue showed small empty vesicles with thin walls, surrounded by scattered lymphocytes and monocytes, a few multinuclear giant cells, partly lining the cysts, supports the view that tissues react to gas somewhat as to the presence of a foreign body.

Singh has stated that oxygen is absorbed slowly from the tissues and may remain under the skin for a week.

Nagashima in 1924 described four museum specimens and two fresh cadavers in the pathological institute of the University of Berlin and pointed out a condition which is present in our first case but not observed in the second. Irregularly shaped interpapillary downward extensions occur, some of which lay in the lamina appropria and are apparently completely separated from the surface epithelium. In some of the down growths of epithelial cells there is a central space partly filled by desquamated squamous cells, erythrocytes and polymorphonuclear leucocytes. Elsewhere the surface epithelium contains several small empty vesicles from 0.5 to 1 mm. in diameter.

He with others believe that the cysts arise primarily in the epithelium, penetrating later into the lymph spaces where gas is formed by bacterial action. He claims to have demonstrated bacteria by special staining methods, the order being penetration of "epithelial nests," liquefaction, cavitation, and gas production.

Our second case shows no downward growths of epithelium but only cysts similar to those described by Dr. Gardner. Their walls consist of fibrous tissue, no epithelial or endothelial lining can be demonstrated. Many flattened giant cells remain along the walls partially lining the cavity, so compressed in certain areas that the nuclei lay in linear order. In the region of the vesicles there is slight infiltration with lymphocytes.

No bacteria were found excepting on the surface and in the most superficial layers of the epithelium.

The origin of the vesicles seem to be by distention of tissue spaces rather than dilation of lymphatic channels. The giant cells are to be considered of histiocytic origin presumably in response to the presence of gas acting as a foreign body. As Dr. Gardner has suggested, these spaces are not true cysts as they do not extend preformed glands or cavities but merely lie within temporary cavities in the interstices of the tissue.

The lack of any marked inflammatory reaction, the failure to recover any single species of microorganism repeatedly from the cysts themselves, the absence of bacteria in stained tissue slides with hematoxylin and eosin, Gram, Giemsa, or Loeffler's methylene blue, excepting on the surface and in the most superficial layers on the vaginal epithelium, our inability to reproduce the cysts in laboratory animals with vaginal secretions, or with any of the bacteria cultivated from the vaginas of these patients suggests that the process is nonmicrobic, and that if bacteria are concerned they do not belong to any of the readily cultivatable and easily recognizable species.

Since we have been unable to demonstrate anything but air in the cysts, we are confronted by the difficult problem of explaining its presence. No physiologic or microbic process is known that would result in the formation of air in the tissues.

It may be that air could be driven into tissue through epithelial defects or gain entrance by way of epithelial down growths which become liquefied, or entering through the cervical glands finds its way along the walls of the vagina. Any of these explanations would sound fantastic.

DR. MILTON A. DARLING, Detroit, Mich.—It happens that I have seen similar cases. The first time I reviewed the literature extensively and found no description of it whatever. I took care of this woman through two pregnancies and the condition appeared in both of them along the posterior vaginal wall, except that the growths were largely on the vagina and did not involve the cervix. Our second case was a nullipara in which the cystic areas largely involved the cervix and vault of the vagina and had no connection with the vaginal floor. The problem in this case was that the woman complained of pain during coitus. It was never determined whether this was the cause as she had other pelvic pathology which could have accounted for pain and discomfort of which she complained.

DR. GARDNER (Closing).—I am glad to hear that others in this audience have seen this condition and I would like to see the cases reported. Various and sundry explanations have been offered by some of the older authors as to how air becomes entrapped in the mucosa of the cervix and vagina. None of their explanations seem logical and I cannot subscribe to any of them. I do not believe that the gas is air and under no circumstances can I see how air could have been entrapped between folds of mucosa or forced into the cervical tissues in the case presented here.

PUERPERAL INVERSION OF THE UTERUS*

HAROLD HENDERSON, M.D., AND RUSSELL W. ALLES, M.D., DETROIT, MICH.
(From the Providence Hospital)

THE subject of inversion of the uterus has been quite thoroughly discussed in the medical literature, yet there still seems to be a lack of unanimity of opinion as to both the cause and treatment of this serious postpartum emergency. The condition is sufficiently rare to make the experience of the average obstetrician inadequate to draw satisfactory conclusions from his own practice. For this reason we have collected a series of twenty-four cases from the records of Providence Hospital, Detroit, over a period of sixteen years. Most of these patients have been personally observed and treated in consultation. They represent an incidence of one in 2,300 deliveries.

It is a significant fact that all but three of the cases were managed by general practitioners, and the patient was not seen by the consultant until her condition became critical. In nearly all cases we were unable to get a history of aggressive management of the third stage, and further evidence of the inaccuracy of the case records is seen in the estimation of blood loss. The figures obtained from the charts probably represent only a fraction of the total hemorrhage. This is particularly apparent in the fatalities where exsanguination and shock were the cause of death.

TABLE I

NO. OF CASES	PARITY		FATALITIES 25%
24	Primigravida	16	2
	Multigravida	8	4
			(All gravida ii)

In this series, the age of the patients varied from 17 to 33. Sixteen were pregnant for the first time and eight were multiparae.

TABLE II. TYPE OF DELIVERY

Spontaneous	18
Low forceps	3
Breech extraction	1
Not recorded	2

There were eighteen spontaneous deliveries, three were delivered by low forceps, one was a breech extraction, and two were not recorded.

*Read before the Central Association of Obstetricians and Gynecologists on Oct. 24, 1947, in Louisville, Ky.

TABLE III. POSITION OF FETUS

Anterior	15
Posterior	2
Breech	1
Not recorded	6

Fifteen were anterior positions, two were posterior, one was a breech, and six were not recorded.

TABLE IV. CLINICAL SIGNS OF INVERSION OF UTERUS

	POSTPARTUM HEMORRHAGE	SHOCK	PROLAPSED UTERUS
Present	20	19	5
Absent	4	5	19

Twenty patients hemorrhaged and in four the blood loss was considered normal. Nineteen patients went into shock and five did not.

TABLE V. LENGTH OF THIRD STAGE

0-30 minutes	13	2 Fatalities
30-60 minutes	2	0 Fatalities
1- 2 hours	2	1 Fatality
2 hours	1	0 Fatalities
Unknown	6	3 Fatalities

The third stage was apparently normal in length of time in thirteen cases, prolonged in five cases, and unrecorded in six.

TABLE VI. TIME OF DIAGNOSIS (AFTER END OF THIRD STAGE)

TIME	NUMBER	FATALITIES
0-30 minutes	10	2
30-60 minutes	1	0
1- 2 hours	2	0
2- 3 hours	1	1
3- 4 hours	1	0
4- 5 hours	2	0
6 hours	1	1
Unrecorded	3	2
7 days	1	0
14 days	1	0
6 weeks	1	0

In ten the diagnosis was made at once and, of these, two died. In eleven cases diagnosis was delayed from one-half to six hours and four patients died. In three other cases, the condition was not recognized until seven and fourteen days, and six weeks, respectively, after delivery. All patients recovered after manual replacement.

TABLE VII. TIME OF DEATH POST PARTUM

Case 1	6 hours, 35 minutes
Case 2	6 hours, 10 minutes
Case 3	3 hours, 34 minutes
Case 5	4 hours, 40 minutes
Case 9	3 hours, 33 minutes
Case 11	5 hours, 55 minutes
Average	5 hours, 5 minutes

The six fatalities all occurred within six hours. The shortest period of time between delivery and death was three hours and thirty-three minutes. This allowed plenty of time for diagnosis and active treatment if the attending obstetrician was alert to the condition of his patient.

From the etiological standpoint, these figures indicate that age of the patient, position of the fetus, and surgical intervention apparently have no influence on the development of inversion. It is significant that sixteen of the twenty-four were primiparas and that in one case, the condition recurred at the next delivery. This suggests a congenital predisposition to inversion, possibly the result of variation in the uterine musculature or its innervation. In five cases, the third stage was prolonged, and in two, a manual removal of the placenta was done. Both of these patients died.

We are forced to conclude, then, that in certain patients there is a predisposition to inversion, and if this is combined with an abnormal or mismanaged third stage, inversion may occur. Therefore, it is our practice to avoid vigorous manipulation of the uterus because it interferes with the normal mechanism of separation and predisposes to retention of placental fragments. It is now our custom to give an ergot preparation intravenously as the child is delivered. The fundus is held, but not massaged unless it relaxes. Massage is accomplished by a rotary motion with the flat of the hand, using the vertebral column as counter pressure. Pressure should not be exerted in the direction of the birth canal. The placenta usually separates in a few minutes, and, as a rule, is expressed before the repair is done. If separation is delayed and general anesthesia is being used, we complete the repair rather than attempt premature expression. We do not like to prolong the use of general anesthesia, but if some form of regional block has been used, we wait for the end of the third stage before reconstructing the perineum.

In this series the problem of diagnosing inversion was complicated by the fact that only five of the cases were accompanied by prolapse of the uterus. In nineteen, the diagnosis had to be made on the basis of shock and hemorrhage, abdominal and vaginal examination. The findings on abdominal examination are unreliable because the inverted fundus is in the normal position in the pelvis, and if the examination is careless or if the abdominal wall is thick, the characteristic dimpling of the uterine tumor is not noted. In not one of these twenty-four cases was this sign of diagnostic value. For this reason, we have made it a rule that in all cases of hemorrhage, with or without shock, a vaginal examination is made at once. The boggy mass of the inverted uterus poses no diagnostic problem if it is looked for. Only ten of our cases were diagnosed promptly, although all patients were treated for shock and hemorrhage. Shock is out of proportion to the amount of blood lost, and this alone should make us suspicious of inversion. This is due no doubt to traction and pressure on the plexus of nerves in the broad ligaments as they are dragged through the hernial opening. If treatment is delayed, the combination of loss of blood and shock may produce a condition so severe that it becomes irreversible and the patient may die despite adequate amounts of blood replacement. Of the six deaths in this series, all patients died within six hours after delivery. All six, however, were given intravenous fluids and five were transfused. These deaths were recorded, two in 1931, one each in 1932, 1935, 1940 and 1941. By present standards of shock therapy, treatment in all cases was inadequate inasmuch as 500 c.c. represented the maximum amount of blood replacement.

The trend in treatment as expressed by the more recent literature is best exemplified by Barrett,[1] who describes three periods in this condition: first, the immediate period when shock and hemorrhage are not too severe and before

sepsis and development of a contraction ring make replacement difficult. Here immediate replacement is advised. Second, the intermediate period, when the above conditions have supervened, and Barrett contends that conservative treatment is indicated. In the late period, when these adverse conditions are under control, replacement is done by an appropriate method.

McKelvey[2] is even more conservative. He treats the shock and hemorrhage and disregards the inverted uterus, treating it some weeks later by an appropriate surgical procedure. Cosgrove[3] reports no deaths in his series in those cases which were promptly diagnosed and replaced. Fatalities occurred only where diagnosis and treatment were delayed. Phaneuf[4] reports five cases treated, one by manual replacement, one by abdominal panhysterectomy and bilateral salpingo-oophorectomy, and three by the Spinelli operation. Harer and Sharkey[5] report twenty-one cases with nine deaths in which mismanagement of the third stage was the chief etiological factor. They employ the immediate replacement of the uterus and make no mention of surgery in their management of this complication.

Das[6] reporting from Calcutta, where inversion seems to be more common than in the United States, advises immediate replacement if possible. If this cannot be done, he recommends treatment of shock and hemorrhage, and, at a later date, the use of the Spinelli operation or the abdominal approach. Salvin[7] observes the much greater frequency of inversion in cattle and emphasizes the point that mismanagement of the third stage may be a less important factor than we have been led to believe. In none of our series were we able to get a history of mismanagement of the placental stage, but it is a significant fact that in only three of twenty-four cases was the patient in the hands of an experienced obstetrician. Stander,[8] in the third revision of his text, advises immediate replacement under general anesthesia, but if shock is severe, he counsels treatment of the shock and hemorrhage before manipulations are undertaken. In chronic cases he advises operation, utilizing the technic of Haultain, Huntington, or Spinelli.

In practically every report in recent years, the treatment of inverted uterus is covered by generalities. Replacement at once if possible is always advised. Treatment of shock and hemorrhage first is usually advocated, with replacement when the patient's condition has improved. Surgical treatment in the chronic stage by several methods is advocated. It is our contention that manual replacement immediately upon diagnosis is not only possible but advisable, being combined of course with vigorous antishock therapy. We feel furthermore that the surgical treatment of this condition is unnecessary in the vast majority of cases, and we point to the fact that we have not used it once in twenty-four cases, and three of these were replaced seven, fourteen, and forty-two days, respectively, after the onset of the condition.

The lack of unanimity in the literature is exemplified in a case recently reported by Reid, Turner, and Summers[9] in which a referred patient was seen three and one-half hours after delivery. She was in collapse and was treated with glucose, plasma, and blood transfusions. Six hours after delivery, vaginal examination revealed an inverted uterus and apparently an unsuccessful attempt was made to replace the organ manually. Two hours later, an abdominal operation was done and the uterus replaced by the method of Huntington under local anesthesia. Despite continuation of active shock therapy, the patient died two days later.

Many cases of inverted uterus are seen by skillful operators who may be confronted with this condition for the first time. Of necessity, they must rely on the consensus of opinion expressed by the literature on the problem of choosing the treatment. Their failure in properly managing these difficult cases

rests on the shoulders of us whose greater experience should guide them in their procedures. Immediate diagnosis of the cause of postpartum hemorrhage and prompt active treatment will save many of these women.

We have attempted to formulate a definite policy of diagnosis and treatment from a study of these twenty-four cases. They cover a period of time during part of which blood banks were unknown and donors had to be found, typed, and cross-matched. Blood was therefore obtained late and in inadequate amounts. Plasma to tide us over while waiting for blood was not available. Four of the patients in first five in this series died, and the last six have all survived. None of the six fatalities received over 500 c.c. of blood, and one was not transfused at all. This indicates that better results in later years are due to improvement in the availability of treatment for shock and hemorrhage. Two of eleven patients diagnosed within an hour died, and three of thirteen died where the diagnosis was delayed. This does not invalidate our plea for early diagnosis, because when shock and hemorrhage are most severe, consultation is called early and diagnosis is more prompt. When the patient's condition is not so alarming, the condition is apt to be overlooked. For example, in our series, in cases diagnosed one, two, and six weeks after delivery, there was no evidence of shock.

All the fatalities occurred within the immediate period referred to by Barrett as the time for active intervention. During this period hemorrhage is continuing and shock is increasing. Blood and supportive measures are not usually enough to combat the condition. The stretching and pinching of the nerve plexus in the broad ligaments and ovaries is sufficient to negate the value of our therapeutic measures. Since replacement at this time is so simple that it can be done in a minute or two and usually without anesthesia, we have adopted the policy of immediate replacement.

To illustrate this point, a 22-year-old para 0 gravida i was delivered normally at 4:10 P.M. with a reported blood loss of 200-300 c.c. She was very restless and at 5:30 was given 1/32 gr. of dilaudid. After this she hemorrhaged profusely and was given ergot and 1,000 c.c. of glucose in saline. Her blood pressure dropped to 60/40 and at 6:50 she was given 500 c.c. of blood. Blood and plasma were continued and oxygen administered. The patient's pulse became imperceptible and respiration stopped. She was being given artificial respiration by means of the gas machine when seen by one of us (H. H.) at 8:30 P.M. At this time blood and plasma were being given into both arms. Examination showed an inverted uterus and it was immediately and easily replaced, and almost instantly her pulse improved and spontaneous respiration started. She made a febrile but complete recovery and became pregnant again two years later.

The replacement of the acute puerperal uterus is simple and usually does not require a high degree of skill. Three of these cases were discovered and replaced by the attending physician or the resident. Ring forceps clamped on the edge of the cervical rim accompanied by traction with counter pressure on the inverted fundus will readily correct the inversion. Packing may be resorted to if necessary to keep the uterus in place, but this is not usually needed. In none of the above cases was there any difficulty in this maneuver, whether it was done by the consultant, the attending physician, or the resident.

A different problem exists in the type of inversion that escapes diagnosis at the time of delivery and is discovered at a later date. Three of our cases fall in this category. One patient who had hemorrhaged moderately, continued to bleed despite ergot, and was unable to void. She was sent to the bathroom on the seventh day and while straining, the entire inverted uterus came out of

the vulva. She was taken to the operating room and under anesthesia the uterus was replaced by the technic of ring forceps on the cervix and manipulation of the fundus. She made an uneventful recovery. Another patient made an apparently normal recovery from a spontaneous delivery and went home on the tenth day. On the fourteenth day, she hemorrhaged and her physician sent her back to the hospital with a diagnosis of placental polyp. Vaginal examination revealed an inverted uterus and under ether, it was replaced by use of the same technic, without a cutting operation.

In the last case of delayed diagnosis the patient hemorrhaged at the time of delivery and was treated by transfusions. She recovered but continued to bleed excessively. Six weeks later she was referred to one of us (R. W. A.) and a diagnosis of chronic inversion was made. Operative interference was considered, but an attempt was made to replace the uterus by taxis. This was successful and she made an uneventful recovery.

Comment

Inversion of the uterus is a serious postpartum complication with a high primary mortality. It is probably more common than the literature indicates and undoubtedly many deaths ascribed to postpartum shock and hemorrhage are due to the concealed variety of inversion. To substantiate this statement, we have the record of a recent case not included in this series, in which death occurred several hours after delivery. Autopsy revealed an inverted uterus. By present-day standards, her treatment for shock and hemorrhage was adequate.

All cases of abnormal postpartum bleeding should be investigated immediately to rule out inversion. Manual replacement should be done at once and not delayed. Transfusions and other intravenous therapy must be carried on at the same time.

Shock is due in part at least to stretching and pinching of the nerve plexus in the broad ligaments, and an integral part of the treatment is directed toward relieving this condition by immediate replacement. Therefore, there is no place in the management of acute puerperal inversion of the uterus for delay in replacement of the herniated organ. Replacement can be made early with little difficulty, by the average operator, without anesthesia in most instances, and without increasing shock.

We have had no experience in the treatment of inversion of the uterus by surgery. Since we have treated patients as late as seven weeks postpartum without either vaginal or abdominal operations, we contend that replacement by taxis is not only possible but preferable in practically every instance.

References

1. Barrett: Illinois M. J. **85**: 253-260, 1944.
2. McKelvey: J. A. M. A. **120**: 679-682, 1942.
3. Cosgrove: Am. J. Obst. & Gynec. **38**: 912-925, 1939.
4. Phaneuf: Surg. Gynec. & Obst. **71**: 106-109, 1940.
5. Harer and Sharkey: J. A. M. A. **114**: 2289-2292, 1940.
6. Das: J. Obst. & Gynaec. Brit. Emp. **47**: 525-548, 1940.
7. Salvin: West. J. Surg. **50**: 147-155, 1942.
8. Stander: Textbook of Obstetrics, Third Revision, New York, 1945, D. Appleton-Century Co., Inc., pp. 967-970.
9. Reid, Turner, and Summers: J. Michigan M. Soc. **46**: 1066-1068, 1947.

3001 W. Grand Boulevard.

Discussion

CURTIS J. LUND, M.D., New Orleans, La.—Two aspects of this uncommon complication of pregnancy are of particular interest. The first is the wide variation noted in the incidence which ranges, according to reports, from 1:740 to 1:16,000 deliveries. At Charity Hospital seven inversions with one death have been observed during the past forty years. The incidence has declined steadily, and at the present time only two cases have been observed in over 90,000 deliveries.

The second point of interest centers about the controversy between (1) those who believe that immediate replacement is an essential part of therapy, and (2) those who postpone replacement for weeks. Divergent as these ideas may be, they have one common denominator which is the treatment of shock.

The results presented today, the results of other investigators as well as our own, indicate that most deaths occur within a few hours and are accompanied by profound shock. Of the few late deaths reported, most are associated with premature attempts at replacement. Deaths from infection have been conspicuously infrequent. Such findings make it obvious that therapy must be focused on shock. With what type of shock are we dealing?

There is little doubt that the shock of the inversion is often out of proportion to the blood lost. The authors attribute this to stretching and pinching of the nerves. This is likely correct and would fit into the classification of primary or neurogenic shock, as described by Blalock, Moon, and others. Such shock is characterized by vasodilatation; it is of short duration and is unaccompanied by hemoconcentration. Uncomplicated primary shock is not especially serious until there is superimposed hemorrhage or secondary traumatic shock. Many of you have seen patients recover partially from the initial inversion only to relapse suddenly into profound and frequently fatal secondary shock. However, in practice the accident is often associated with postpartum hemorrhage so that the primary shock is obscured and no recovery period is noted.

It is the secondary or traumatic shock which kills unless quickly and adequately treated. We cannot overemphasize that adequate treatment usually requires enormous amounts of blood and plasma as it is not unusual to find hemoglobin levels of 4 or 5 Gm. after the initial shock and its hemoconcentration has been overcome.

It would appear that the real value of immediate replacement lies in the treatment of primary neurogenic shock. This stage is relatively short so that the effectiveness of reposition becomes inversely proportional to the duration of the inversion. For this reason we believe that immediate replacement should be limited to those patients (1) who can be treated within two or three hours of the inversion, (2) upon whom replacement is readily performed without deep anesthesia or extensive manipulation, and (3) who are not exsanguinated or in serious secondary shock. It must be clearly understood that successful reposition in no way eliminates the need for vigorous therapy of shock.

Those who advocate conservative therapy have clearly shown that death can be virtually eliminated but at the cost of prolonged and vigorous therapy. Successful immediate replacement can be followed by a rather short and uneventful convalescence in carefully chosen patients, but it must not become a factor contributing to the mortality of the disease.

DR. PALMER E. SUTTON, Royal Oak, Mich.—At the risk of some repetition I wish to make a few observations. Puerperal inversion of the uterus has occurred at Woman's Hospital in Detroit eight times since 1929; eight times in 47,576 deliveries, an incidence of 0.0168, without mortality. I would like to contrast this incidence and this result with the incidence in one other institution where puerperal inversion has occurred only once in a series of 1,679 deliveries with one death. The combined incidence is 9 cases in 49,000 deliveries.

As Dr. Henderson and Dr. Lund have pointed out, gravidity, parity and other such factors do not seem to enter into the problem. In all nine instances the cases were those of

uncomplicated labor. According to the charts there was no complication in the first stage. The condition occurs rarely in the practice of any physician. In these nine cases it never occurred more than once in the practice of any one individual. Five of the cases occurred in the practice of individuals with limited obstetric preparation; two were staff cases and were delivered by residents or interns. Four of the nine were recognized immediately or very early and had no morbidity. It was interesting that in this group of four without morbidity one of the cases was observed following manual removal of the placenta at the time of cesarean section. It was immediately corrected. It is also interesting to observe that one of these cases was immediately replaced presumably and packed and the patient returned to her bed; she continued to bleed and was brought back for re-examination. The consultant took her to the operating room and did a laparotomy and found the first operator had perforated the uterus, so hysterectomy was done. She had no postpartum or postoperative morbidity. In the cases with postpartum morbidity it was not in excess of five days. Discovery of the condition was immediate in two cases and the cases were treated by replacement, transfusion, and treatment for shock. One of the cases with morbidity was not discovered until the patient had been in her room for two or three hours and continued to bleed. She was brought back and examined. The consultant did a laparotomy, replaced the inversion by abdominal route and sutured the uterus to the abdominal wall, bringing the suture out through the wound and tying it over a glass rod. I mention this as an unusual method of treatment. One of the cases of morbidity was discharged on the tenth day but at home continued to bleed. After six weeks she was brought back and operated abdominally. This was a chronic inversion. She was treated by fixation of the uterus and sterilization. The woman who died is one from which we should draw considerable conclusions. It occurred in a small institution where there are no interns or residents. There are facilities for blood transfusion. The attendant had never seen inversion before. As soon as it was discovered that she was bleeding he called for help and it happened that I was the one he called. I was, however, in attendance on another patient in another hospital and he finally obtained the help of a general surgeon who came in and took her to the operating room; the inverted uterus was amputated and the patient put to bed. While efforts were still being made for transfusion she died. Because of the occasional experience that puerperal inversion of the uterus occurs and is not discovered until the patient has gone back to her room, many of us have felt that routine examination of the cervix with a retractor and ring forceps is a worth-while procedure to prevent the occasional unrecognized puerperal inversion.

DR. RUDOLPH W. HOLMES, Charlottesville, Va.—Drs. Henderson and Alles must be congratulated on their unique experience with 22 cases of puerperal inversion seen in consultation. In the last century inversion was estimated to occur once in 100,000 labors; by Hirst once in 140,000; in the Rotunda once in 190,000, and none in Carl Braun's services in 250,000 labors. That inversion has been reported more frequently these late years is indisputable: that the anomaly is more frequent these days, due to a devitalization of the uteri of modern women, is manifestly a spurious implication. We must believe that in times long past few women were examined post partum, so the inversion was not discovered: in our modern world the routine post partum, and follow-up examinations, gives us an increased incidence due to discovery alone.

It was a vicious preachment that inversion was due to mismanagement on the part of the attendant, for I am firmly convinced that it is more the result of malign forces within the uterine body (is spontaneous in origin) rather than brusque Dublin or Crede maneuvers, or other mechanical forces. In a collaborated text book some forty years ago, under inversion, it was stated that inept conduct of the third stage was the responsible cause: under treatment of the third stage the recommended procedures were so crude most women who were so treated would have had inversions if it were not for inherent abnormalities in the uterus itself.

So far as I know no one has added anything to the mechanics of inversion since Barnes and Radford expounded their theories for the mechanics. The production of an inversion by eversion of the uterine wall (Taylor's mechanism) is probably of pure historic interest,

which is comparable to the process of the dunging of a horse. The true mechanism presages a softened, relaxed area at or near the fundus: the rim of the depression contracts which forces the introcedent wall downwards: as the depressed wall descends, in turn, lower areas of the uterine wall contract and force it down lower and lower until the inversion is completed. This mechanism is the key-note in the method of replacement. That a grossly relaxed, atonic uterus may be forced out by abdominal pressure may be unquestioned.

The fundamentals of treatment comprise these steps: (1) Immediate reposition on discovery, with or without anesthesia: remove the placenta (if still adherent) only after first attempts are futile: (2) The replacement must progress in the inverse order to that which occurred in the production—i.e., that which inverted last must be returned first, until the fundus has returned to its normal situs. By this method only *two* thicknesses of the introcedent wall pass through the cervix: the attempt will usually fail if the fundus is first forced upward as thereby *four* thicknesses must necessarily be crowded through the cervical canal. (3) After reposition, whether there be hemorrhage or not, the uterus and vagina must be firmly tamponed. A mere vaginal tampon is an absurdity. (4) Shock and hemorrhage must be combated.

In line with what has been stated the placental implantation is commonly found near or at the fundus.

DR. E. W. FISCHMANN, Chicago.—In inversion we usually describe three varieties. In the first, there is a depression or cup-shaped depression of the fundus. In the second, the fundus of the uterus comes through the cervix but does not come down into the vagina. The third variety is complete inversion. I think it is important to make an abdominal palpation on all cases immediately post partum. I have seen several cases in consultation where the condition was not recognized for several days post partum because there was no such abdominal examination made.

I want to ask the essayist how he treats the cases in regard to the placenta. Complete inversion of the uterus occurs in some cases where the placenta is still attached to the fundus or the interior of the uterus. We have had success by using small doses of adrenalin injected into the uterine musculature prior to any attempt at immediate reduction.

The essayist mentioned one case in which subsequent pregnancy occurred after inversion. We have had three cases in which the patient has had a subsequent pregnancy, and in one case two subsequent pregnancies, so all cases of inversion of the uterus are not necessarily followed by morbidity or conditions which may prevent subsequent pregnancy. Furthermore, inversion of the uterus does not recur in subsequent pregnancies. I have scanned the literature rather carefully and have found no such cases reported.

DR. HENDERSON (closing).—The experience of Dr. Lund and Dr. Sutton is similar to ours. I also work in two hospitals. In Harper Hospital we found several cases over a period of years while in the Providence Hospital, where a large part of the work is done by local practitioners, the incidence has been appalling. As the hospital staff has changed to younger and better trained men, the incidence of inversion of the uterus is greatly decreased.

As Dr. Lund has said, there are two types of shock in this condition; one is the result of hemorrhage and the other the result of trauma. We can increase traumatic shock by manipulation, but those same manipulations can be done in such a way as not to increase the shock. That brings up the point of the technic of replacing the uterus. Dr. Holmes has emphasized that the uterus must be replaced in the same order in which inversion occurred, and that if you push the fundus back, you have four layers of uterine wall to go through the cervix. If you remember that, and take hold of the cervix with ring forceps, and push the fundus with a little traction on the cervix, you will find it will go back in the same way it comes out. That is why we have had success in our treatment.

Listening to Dr. Sutton's discussion emphasizes our reasons for being insistent on the more conservative management of this condition.

Dr. Fischmann described the three varieties of inversion. The first type is not usually discovered because in most instances it goes back spontaneously. In our series, nineteen were complete inversions but not exteriorized. Dr. Fischmann also asked about the placenta. In one of our cases the uterus came out with the placenta in place. We decided the best thing to do was to replace the uterus with the placenta intact, which we did, and then very carefully watched the third stage. It was not long before the placenta came out. He advocated the use of adrenalin. We have not had success with it.

So far as recurrence is concerned, we had three inversions during the last year which had occurred elsewhere, and the women came to us in a subsequent pregnancy, one of them being pregnant for the second time following inversion. We have delivered all three of them without difficulty and without recurrence of the inversion. We were looking for a recurrence and managed the third stage with that in mind.

ACUTE ANTERIOR POLIOMYELITIS IN PREGNANCY*

E. Stewart Taylor, M.D., and Jack M. Simmons, Jr., M.D., Denver, Colo.
(From the Department of Obstetrics and Gynecology, University of Colorado School of Medicine)

DURING the summer and fall of 1946, there were nine hundred new cases of poliomyelitis reported in Colorado. Of these, one hundred thirteen were among women between the ages of seventeen and forty. Of the twenty-five who were pregnant, seventeen were treated by the staff of the University Hospital.

It has been estimated that 11.7 per cent of Colorado's women between seventeen and forty were pregnant on any given day during the epidemic. Twenty-two per cent or twice as many of the poliomyelitis victims in the same age group were pregnant. Our experience corresponds with that of others,[1-4] who have suggested that pregnant women have a predilection for poliomyelitis. Our incidence of poliomyelitis during pregnancy has been subjected to statistical analysis and has been demonstrated to be significant (the standard error between the two groups is 3.5). This analysis also indicated that a pregnant woman in Colorado during this period had one chance in a thousand for contracting the disease.† What are the answers? Why does it happen? Let us review the experience gained from our epidemic.

Epidemiologic Aspects

Of the twenty-five acute poliomyelitis cases accompanied by pregnancy, eight appeared in the first trimester, eleven in the second, and six in the third. Each of the nine months was represented.

In another study, Aycock[1] summarized two hundred thirty-six cases with pregnancy and poliomyelitis and found the distribution of cases as follows: fifty-three in the first trimester, ninety in the second, and ninety-one in the last.

Although the pregnant woman in Colorado during the epidemic seemed to be twice as susceptible to the virus as her nonpregnant sister, there were some compensations if she contracted the disease during the first two trimesters of pregnancy. Of nineteen patients in the first and second trimesters, there were no fatalities, and only two of the nineteen have significant residual paralysis (see Table I). On the other hand, of eighty-eight nonpregnant, seventeen to forty-year-old women who had poliomyelitis during the same epidemic, 66 per cent had the paralytic form of the disease and seven of these patients died of bulbar poliomyelitis. Perhaps there is something about the first six months of pregnancy that makes the disease more easily contracted and yet a milder one.

The six patients who fell ill during the last three months of pregnancy had a very different and tragic course. During the last trimester, the prognosis is terrifying. There were three deaths from bulbar paralysis. A fourth bulbar

*Read before the Central Association of Obstetricians and Gynecologists on Oct. 24, 1947, in Louisville, Ky.

†The calculations were made by Dr. Lloyd Floris, Professor of Public Health, University of Colorado School of Medicine.

case was a near fatality upon numerous occasions. After twelve months, she is still in a respirator and has quadriplegia and diaphragmatic paralysis. Two more patients have severe residual extremity paralysis. These results contrast sharply with the recoveries experienced by early pregnancy patients, in whom only two out of nineteen suffered permanent damage. Although the series is small, the mortality rate of 50 per cent in the last trimester greatly exceeds that of 6 per cent for the entire Colorado epidemic and 8 per cent for the eighty-eight nonpregnant women in the age group under consideration. The difference between the course of poliomyelitis contracted early in pregnancy and that occurring during the last trimester is striking.

Support for the validity of this observation was obtained by a re-examination of previous reports of coincident poliomyelitis infection and pregnancy. We were able to collect from many sources one hundred seventy additional cases in whom the trimester of pregnancy and the course of the disease were known.[2, 3, 5-12] Weaver and Steiner[5] in 1944 provided in their article an extensive tabulation of cases bearing upon the subject. Grelland[6] in 1947 summarized similar data for fifty-eight cases in the Scandinavian literature. None of these series was large enough to indicate the extreme difference in prognosis for early and late pregnancy. However, when examined collectively, it is apparent that our data are significant. Of one hundred ten first and second trimester patients, there were eight deaths or a 7 per cent mortality rate. On the other hand, among eighty-five last trimester cases, twenty-three patients or 27 per cent died from bulbar poliomyelitis.

Some writers have said that hormone changes influence susceptibility to the virus of poliomyelitis.[13-17] Animal experiments have suggested that increased estrogen titer is protective to a host attack by the disease.[13, 14] Our clinical evidence refutes such a hypothesis for, during late pregnancy when women are most abundantly supplied with estrogen, their resistance to the virus is poorest.

Anderson,[14] experimenting upon mice infected with a murine type of polioencephalitis virus, was able to demonstrate the protective nature of both estrogen and progesterone. We know that progesterone is present in its largest amounts during the last months of pregnancy. The body stores of progesterone and estrogen do not protect the last trimester pregnant woman from the virus.

Chorionic gonadotropic hormone has been said to be protective against poliomyelitis.[5, 16,17] There is some experimental basis for such thought.[5, 17] If this were true, it should be particularly so during early pregnancy when its titer is highest. Actually, the incidence of poliomyelitis at this time is greater than in the normal population. Further, we know that this hormone remains in the blood until the end of pregnancy, even if in reduced amounts. It is difficult, then, to reconcile its value when late pregnancy cases with measurable amounts of the gonadotropin fare so poorly.

Notwithstanding, it is obvious that the manner in which poliomyelitis afflicts pregnant women differs greatly from its effect upon other segments of the population. According to our observations, patients who contract poliomyelitis before the seventh month of pregnancy are likely to recover with little or no paralysis. The recovery seems to take place in spite of an increased susceptibility. Estrogen and progesterone might then be considered protective in early pregnancy. What happens during the last trimester? The progressive rise in estrogen and progesterone is conveniently coincident with the sudden appearance of serious disease in the last months. These two hormones may have been protective during early pregnancy but in the last months the increased amounts of estrogen and progesterone would have to be virucidal to such a marked degree that a Herxheimer-like reaction is produced. Extensive inflammation, edema, and necrosis of anterior horn and bulbar nuclei cells may be

precipitated. This sudden and massive destruction of the neurotropic virus and the accompanying profound tissue response may account for the severity of the disease in late pregnancy. Such an explanation will reconcile animal experiments and clinical observations.

The changes in hormone metabolism fail to explain the increased incidence of poliomyelitis among pregnant women. Two factors seem important to us. One is that pregnancy produces a congestion and increased permeability of the upper respiratory and upper digestive tracts. Such a condition may provide a more advantageous port of entry for the virus. A second factor that may play a role is chronic fatigue. In nonpregnant individuals, this has been observed to be a predisposing factor to poliomyelitis.[18-21] Pregnancy in its last half means a state of chronic fatigue for most women. The favorable portal of entry and the fatigue element appear to be factors that increase the pregnant woman's susceptibility to the disease.

Obstetric Aspects

Our obstetric experience during the epidemic was interesting. The woman near term is a special problem. As we have shown, the patient usually has a severe form of the disease. Although our results are very poor for the mothers in the last trimester, one cannot see how interruption of the pregnancy will improve the prognosis. In one case, there was slight involvement until after delivery, at which time, the condition became much worse. During the acute infectious phase of bulbar poliomyelitis, a woman in her last trimester of pregnancy is a grave risk for any operative procedure.

We have delivered or had reported to us the obstetric end results of all of the twenty-five cases. Two of the twenty-five aborted early and at the time of their acute infection. There were no cases of poliomyelitis in the newborn, or congenital deformities. There were two sets of twins. Twenty-four viable infants have been delivered, thirteen male and eleven female. As has been adequately demonstrated in the past,[22, 23] the degree of maternal spinal paralysis had no serious effect upon the labor. The uterine contractions proceeded in labor at term just as in a nonparalyzed patient. The mother's voluntary efforts at expulsion of the fetus were ineffectual in some cases due to paralysis. In this type, a low forceps operation was used as a substitute. We noticed three lower extremity paralysis cases were unable to walk until after delivery. The pregnancy had upset the skeletal balance and prevented reeducation of muscle groups. We performed postmortem cesarean sections on two women who died of bulbar poliomyelitis, one at the thirty-second week and one at the thirty-seventh week of pregnancy. The first had twins, one of which was born dead, the other liver but died of pneumonia eighteen days later. A third baby, from the second mother, survived and is normal. A poliomyelitis infection during the last weeks of a pregnancy carries as grave a maternal prognosis as can befall a patient.

Summary

During Colorado's 1946 poliomyelitis epidemic, twenty-five cases of pregnancy with acute poliomyelitis were observed. The combination of pregnancy and poliomyelitis occurred twice as frequently as was statistically anticipated. The twenty-five cases were followed through delivery. There were no cases of congenital disease in the newborn. Poliomyelitis had no serious effect upon the labors of the victims. A study of our material and a study of one hundred and seventy similar cases reported by others showed that during the first six months of pregnancy, one hundred ten patients had a 7 per cent mortality

rate while eighty-five last trimester cases had a 27 per cent mortality rate. This difference in severity of the disease during late pregnancy is striking. It is suggested that the increased permeability of the upper respiratory and digestive tracts to the poliomyelitis virus during pregnancy and the fatigue of pregnancy are important in accounting for the increased incidence of the disease. Nineteen of our patients, who fell ill during the first six months of their pregnancy, had no mortality and suffered none of the severe paralytic end results of the disease. However, our six last trimester of pregnancy cases did very poorly. Three of them were fatalities and three developed permanent severe paralysis. Perhaps, estrogen and progesterone are protective to the pregnant poliomyelitis victim early in pregnancy. In the last trimester of pregnancy, these hormones are not protective. However, they may be virucidal to such a profound degree that a Herxheimer-like reaction is created within the host, causing irreversible tissue damage.

Table I summarizes each of our twenty-five cases. It will be noted that these patients are arranged according to their week of pregnancy. The two right-hand columns on the table show that the more advanced the pregnancy, the more grave the prognosis for the poliomyelitis.

TABLE I. SUMMARY CHART OF 25 ACUTE POLIOMYELITIS AND PREGNANCY CASES

PATIENT	AGE	PARITY	DELIVERY	INFANT	WEEKS OF PREGNANCY AT ONSET	POLIOMYELITIS RESIDUAL
M. H.	29	2	Spontaneous	Normal M.	4	None
C. A.	17	0	Spontaneous	Normal F.	4	None
R. W.	25	2	Spontaneous	Normal F.	6	None
J. P.	24	0	Spon. abortion, 7 weeks	?	6	Mild
N. L.	25	3	Spontaneous	Normal M.	6	Mild
L. M.	24	1	Spontaneous	Normal F.	10	None
E. T.	39	6	Spontaneous, twins	Normal M. & F.	11	None
B. F.	32	1	Spontaneous	Normal M.	12	None
R. M.	25	1	Spontaneous	Normal F.	13	Moderate
H. A.	33	2	Spontaneous	Normal M.	14	Minimal bulbar
E. J.	27	1	Spontaneous	Normal M.	15	None
P. Y.	19	0	Spon. abortion, 20 weeks	Male	19	None
C. S.	22	2	Spontaneous	Normal M.	19	Minimal Bulbar-spinal
D. H.	22	0	Spontaneous	Male; died, 28 hr., pneumonia	19	None
I. M.	19	1	Low forceps	Normal F.	21	Moderate
B. B.	22	0	Assisted breech	Normal F.	22	Mild
M. M.	29	1	Spontaneous	Normal M.	23	Mild
L. G.	27	0	Spontaneous	Normal M.	26	None
L. J.	24	0	Spontaneous	Normal F.	28	None
B. S.	17	0	Low forceps	Normal M.	29	Severe
J. W.	19	0	Spontaneous	Normal F.	31	Fatal bulbar
L. S.	23	2	Postmortem section	Normal F.	32	Fatal bulbar
F. T.	28	3	Spontaneous	Normal M.	36	Severe
F. C.	31	5	Postmortem section, twins	M. & M. 1 stillborn 1 died, 18 days, pneumonia	37	Fatal bulbar
A. H.	33	1	Midforceps	Normal F.	39	Very severe Bulbar-spinal

Figs. 1, 2, and 3 summarize the paralytic and mortality rates observed as part of the study.

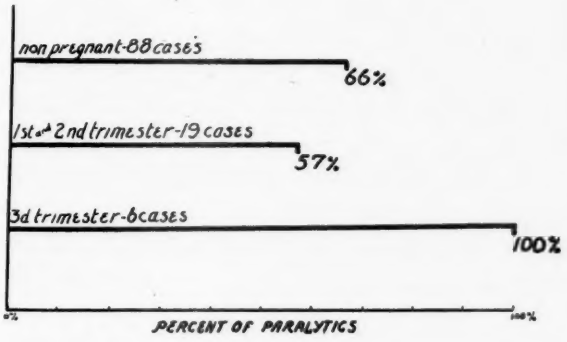


Fig. 1.

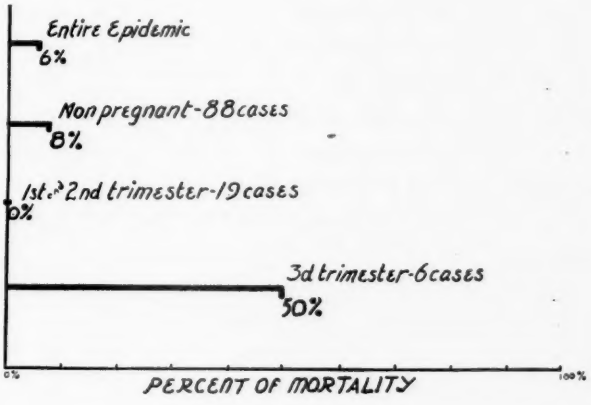


Fig. 2.

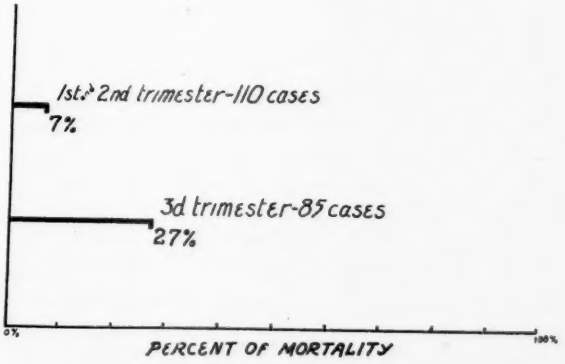


Fig. 3.

Fig. 1.—Poliomyelitis, paralytic rate, Colorado, 1946.
Fig. 2.—Poliomyelitis epidemic. Mortality rate for Colorado, 1946.
Fig. 3.—Poliomyelitis in pregnancy, mortality rate for 195 cases.

Conclusions

1. During the 1946 poliomyelitis epidemic in Colorado, the pregnant woman was twice as vulnerable to the virus disease as the nonpregnant woman of the same age group.

2. This does not mean that pregnancy should be avoided during an epidemic. The pregnant woman's chance of contracting poliomyelitis was one in one thousand. The nonpregnant woman of the same age group was exposed to an incidence of one in two thousand.

3. Women in all months of pregnancy were equally susceptible to poliomyelitis in our series.

4. During the first two trimesters, the prognosis for recovery is excellent.

5. Poliomyelitis acquired during the last trimester carries a serious prognosis for life of the mother or for escape of severe permanent paralysis.

6. Hyperemia and congestion of the upper respiratory and upper digestive tracts and fatigue of pregnancy are offered as possible explanations for the increased incidence. However, there are probably other factors at work which are more important but unrecognized.

7. Estrogen and progesterone may be protective to a poliomyelitis victim early in pregnancy. This is not true in the last trimester.

8. The virus does not pass the placental barrier. All children born of mothers infected during this epidemic have been free from congenital disease.

9. Management of pregnancy accompanied by acute poliomyelitis in the last trimester of pregnancy is a challenging problem. The policy to follow in any given case is a difficult decision. In the acutely ill patients, cesarean section seems unreasonable.

10. Poliomyelitis had no ill effects upon the progress of labor except that it necessitated an occasional forceps operation.

References

1. Aycock, W. L.: New England J. Med. **235**: 160, 1946.
2. Aycock, W. L.: New England J. Med. **225**: 405, 1941.
3. Waaler, E.: Acta med. Scandinav. **123**: 209, 1946.
4. Netteblad, A.: Nord. med. **18**: 657, 1943.
5. Weaver, H. M., and Steiner, G.: Am. J. Obst. & Gynec. **47**: 495, 1944.
6. Grelland, R.: Nord. med. **33**: 620, 1947.
7. Fox, M. J., and Sennett, L.: Am. J. M. Sc. **209**: 382, 1945.
8. Biermann, A. H., and Pisczek, E. A.: J. A. M. A. **124**: 296, 1944.
9. Harmon, P. H., and Hoyne, A.: J. A. M. A. **123**: 185, 1943.
10. Roper, L. J.: Personal Communication, Dept. of Health, Richmond, Va.
11. Horstmann, P., Ipsen, J., and Lassen, H. C. A.: Nord. med. **30**: 807, 1946.
12. Guttmann, L.: Med. Klink. **29**: 939, 1933.
13. Aycock, W. L.: Endocrinology **27**: 49, 1940.
14. Anderson, J. A.: Publication of the Rocky Mountain Conference on Infantile Paralysis, p. 15, Dec. 16 & 17, 1946, Denver, Colo.
15. Jungeblut, C. W., and Engle, E. T.: J. Immunol. **24**: 267, 1933.
16. Jungeblut, C. W., and Engle, E. T.: J. Exper. Med. **59**: 43, 1934.
17. Jungeblut, C. W., Meyer, K., and Engle, E. T.: J. Immunol. **27**: 43, 1934.
18. Levinson, S. O., Milzer, A., and Lewin, P.: J. Hyg. **42**: 204, 1945.
19. McCormick, W. J.: M. Rec. **155**: 89, 1938.
20. deRudder, B., and Petersen, G. A.: Klin. Wchnschr. **17**: 699, 1938.
21. Brown, G. C., Francis, T., Pearson, H. E.: J. A. M. A. **129**: 121, 1945.
22. Kleinberg, S., and Horwitz, T.: Surg., Gynec. & Obst. **72**: 58, 1941.
23. McGoogan, L. S.: Am. J. Obst. & Gynec. **24**: 215, 1932.

Discussion

DR. C. P. HODGKINSON, Detroit, Mich.—Acute anterior poliomyelitis as a complication of pregnancy is a relatively new obstetric problem. Subsequent to Schell's report in 1906, a number of papers have been published, the majority of which have been case reports, or collective reviews. Crystallization of thought has been hampered by lack of experience. The paper by Drs. Taylor and Simmons helps fill the gap in clinical knowledge by substantiating in some instances and discrediting in others impressions formulated from piecing together case reports. Their findings are based upon experience in an unusually severe epidemic of acute anterior poliomyelitis in a relatively confined area over a short period of time. No other report approaches this either in concentration of observation or in the number of cases reported. Such circumstances give the obstetrician a more complete and clear-cut picture of what can be expected when a patient develops acute anterior poliomyelitis. The increasing importance of this problem is emphasized by epidemiologic statistics, which show that there has been a gradually but definitely increased incidence of poliomyelitis among older age groups over the last fifty years. Dr. Taylor does not mention the percentage of adults affected in the Colorado epidemic of 1946, but apparently it was high, as 113 women between the ages of 17 and 40 were reported.

It early became apparent that four pertinent questions arose in the minds of obstetricians when their patients became infected with the virus of poliomyelitis. The consistent experience of all demonstrated that the maternal infection did not affect the baby. Moreover, the progress of the pregnancy or delivery was not materially influenced. The third question, whether the pregnancy influenced the usual course of the disease, is of special importance. Sabin, in a recent paper on poliomyelitis, stated, "One of the most important and difficult jobs in science is to ask the right question of nature." The mild course of the disease in the first two trimesters and the unusually severe course in the last trimester are difficult to correlate. Is this due to a break in immunity or to an exaggeration of the disease by the altered physiologic state of the last trimester of pregnancy? Immunologic studies are confusing, in that they have shown the sera of pregnant women to be more resistant to the poliomyelitis virus, and clinical studies are not consistent with the thought that the altered endocrine status decreases susceptibility. As pointed out by Drs. Taylor and Simmons, when estrogen and progestin blood levels are the highest, the disease is most severe. Moreover, it appears that chorionic gonadotropin is not protective. Is the increased intracellular fluid, more characteristic of the last three months of pregnancy, a factor in contributing to the more extensive and rapid death of the anterior horn cells? The additional localized edema incited by the presence of the virus in the spinal cord may aggravate greatly the severity of the disease. Drs. Taylor and Simmons suggest a Herxheimer-like reaction to explain this increased virulence. The last major point is the apparent increased frequency during pregnancy. Here, again, the picture is clouded by many unexplained variables. Epidemiologists are unable to explain adequately the cause for epidemics. The mode of transmission of the virus, the seasonal variation of the disease, and the problems of immunity are poorly understood. Estimation of the actual incidence of the infection is pure guesswork because of the high ratio of abortive to frank cases. Pregnancy further complicates the problem and one wonders if the increase in frequency is not more apparent than real. Are there actually more pregnant women infected or does the state of pregnancy convert abortive to frank cases when the immunity barriers are violated? Drs. Taylor and Simmons mention chronic fatigue and congestion of the upper respiratory and gastrointestinal tracts as possible important factors. Until further studies clarify these points, they must remain in the field of speculation.

DR. WILLIAM J. BLACKWELL, Evanston, Ill.—Anterior poliomyelitis is no longer the exclusive concern of the pediatrician and the orthopedist. In the last few years, an increasing percentage of the adult population has been affected, until the disease has now forced itself to the attention of the obstetrician.

The occurrence of poliomyelitis in pregnancy is so infrequent that the increased dangers may not be recognized. The very fine presentation of Drs. Taylor and Simmons' study is

most convincing that acute poliomyelitis assumes a more serious aspect when it is associated with pregnancy.

We have admitted six gravid women to Evanston Hospital in the last two years with acute anterior poliomyelitis. Three, who were in their second month of pregnancy, recovered completely. Of these, two aborted within a week of admission. The third delivered a normal male infant at term.

Of the other three, two were in their last six weeks of gestation. One of these has a residual paralysis of the left arm, but delivered a normal female infant without difficulty. The second entered the hospital with respiratory embarrassment and died six hours later. Fetal heart tones were absent on admission and the postmortem examination revealed no evidence of poliomyelitis in the fetus. It would appear that the disease is not transmitted from the mother to the fetus.

The sixth patient developed paralysis of her legs twenty-four hours post partum. She was in the respirator for four weeks and was left with a residual quadriplegia.

One of this group had been a nurse on the contagious floor the previous year (1946) when the epidemic of poliomyelitis had been quite severe. She remained in good health, but this year, when she was no longer working in the hospital, she contracted the disease when two months pregnant. Certainly one may suspect that pregnancy increased her susceptibility to poliomyelitis.

Three of the six patients contracted poliomyelitis in the first trimester of pregnancy and recovered, although two of the three aborted.

The group who developed poliomyelitis in the last trimester of pregnancy had a much more severe form of the disease—one died, the other two have residual paralysis.

These findings are in agreement with the conclusions of Drs. Taylor and Simmons' excellent essay.

DR. LEON McGOOGAN, Omaha, Neb.—I became interested in this in 1932, at which time I saw three cases. My total experience since then has been seventeen cases of pregnancy complicated by acute anterior poliomyelitis, ten of which were seen in the Nebraska epidemic of 1946. Of this group of ten cases, one case appeared in the first trimester, six in the second, and three occurred in the third trimester, again showing a general distribution throughout the three trimesters of pregnancy. One of the patients was a primipara; the rest were multiparas.

So far as the obstetric experience is concerned, one patient miscarried, one delivered prematurely at 34 weeks; the baby was normal and survived. One died at five and a half months because of bulbar paralysis. One patient died seven and a half months pregnant, undelivered; postmortem cesarean section was performed but the baby died. The rest of the patients delivered without difficulties and without evidence of poliomyelitis appearing in the child.

As to the reason why these women are more susceptible, may I ask Dr. Taylor a question? We know that metabolism is increased during pregnancy. Is there an increased percentage of growth hormone present in pregnancy? Is it possible that the combination of increased metabolism and increased growth hormone might be an explanation as to why a pregnant woman is more susceptible to the disease?

I had in my series two postmortem cesarean sections. Both women were at the period of viability. Both had been in a respirator for from twenty-eight hours to five days. During that time they were subjected to toxemia from the pathology of the disease. Should we, for the sake of the baby, wait until the patient is moribund and then do a cesarean section, or should we do a cesarean section before the patient is placed in the respirator? By that time the prognosis is bad for the mother anyway. Could this be done under local anesthesia without any effect on the progress of the disease and with some hope of saving one of the two members?

DR. CHARLES NEWBERGER, Chicago.—I want to make the following case report. The patient, a 22-year-old primipara, was cared for prenatally in the outpatient department of Mt. Sinai Hospital. She was admitted to the hospital in September, 1938, in labor at term,

with breech presenting, apparently a normal individual. During the course of the day respirations became labored and she developed paralysis of the limbs and the abdominal muscles. Consultation was called, and a diagnosis of acute anterior poliomyelitis was made. The difficulty in breathing increased, and the patient was placed in a respirator. Her labor progressed rather rapidly and so did her complicating symptoms. Heart tones were good.

We knew that this patient could not be out of the respirator for any length of time; it was found that about a minute and a half were the most she could go on breathing without the use of a respirator. Dilatation came to completion but there were no expulsive efforts on the part of the patient because of the paralysis of the abdominal muscles. We, therefore, had to plan to deliver this woman outside the respirator within a period of not more than ninety seconds. We organized a crew of about ten people. Each one was assigned a very specific task, two to hold the legs, one to do the extraction, one to handle the forceps for the aftercoming head, one to clamp the cord, one to deliver the placenta, one for the intravenous Ergotrate. We arranged for someone to get spinal fluid and one for blood transfusion. However, by the time delivery of the baby was carried out in accordance with our plan, there was not sufficient time to carry out some of the other work. We got a live baby and the mother was hurried back into the respirator. She appeared a little better after the birth but within twenty-four hours she died from a severe form of bulbar paralysis. Our pathologist said that he had never seen such destruction of tissue as he saw in that patient. The infant survived. I saw the baby when he was 4 years old.

I thought it would be of interest to cite the unusually dramatic situation which challenged our management of this labor.

DR. TAYLOR (Closing).—The observation has been made that poliomyelitis is not a childhood disease any more but is becoming a disease of the adult population. Strangely enough, the Public Health authorities through some means are able to predict where an epidemic will be.

As to Dr. McCoogan's suggestion of increased metabolism and increased growth hormone having something to do with the problem, I do not know. Someone else will have to work that out. I would not do a cesarean section before anticipated death in these patients because there have been some cases that battled it out in a respirator for a few days and then finally made a complete recovery.

It is apparent that there is increased danger of poliomyelitis infection during pregnancy. However, you can reassure your young women that they have 999 chances out of 1,000 of missing the infection.

Dr. Baker, the neurologist from the University of Minnesota, came out to Denver to be of aid. He did not wait until patients showed signs of cyanosis and the respirations were difficult before doing a tracheotomy. He took all the bulbar cases that he thought were going to do poorly and did an elective tracheotomy and got a flow of oxygen into the patient before cellular destruction had taken place in the stem of the brain. His treatment will improve the prognosis in bulbar poliomyelitis.

The discussants have all emphasized how dangerous a disease poliomyelitis is during the last months of pregnancy.

PROLAPSE OF THE VAGINA FOLLOWING ABDOMINAL HYSTERECTOMY*

DAVID A. BICKEL, M.D., SOUTH BEND, IND.

(From the Memorial Hospital)

VAGINAL prolapse following hysterectomy is relatively rare in proportion to frequency of that operation. Although the condition is not a common occurrence, it is seen frequently enough to interest gynecologists in its prevention and cure. It has been very rarely observed following hysterectomy operations which have been performed in more recent years, and especially by surgeons who pay particular attention to pelvic surgery. There is still some difference of opinion as to the type of hysterectomy, total or subtotal, which is most likely to be followed by prolapse of the vagina. It has occurred following both types of hysterectomy, and it has been believed that removal of the cervix with severance of its supporting ligaments predisposes to prolapse of the vaginal vault. However, it is probable that factors other than the removal of the cervix are distinctly involved in this condition.

Material

The material for this study consisted of 16 cases of prolapse of the vagina, all following subtotal abdominal hysterectomy. Patients with enterocele of the posterior cul-de-sac alone following vaginal hysterectomy are not included in this group, only cases of prolapse of the vaginal vault. These cases were observed in private and hospital practice over a period of seventeen years. During this period, no such cases were observed following either total abdominal or vaginal hysterectomy. A similar, and more extensive observation, was made by McKinnon and Counseller.[1] In 24 cases of postoperative vaginal herniation, they found that 23 followed the incomplete operation and only one followed total hysterectomy.

In none of the cases reviewed in this report was the hysterectomy performed by a gynecological surgeon, or one especially interested in pelvic surgery.

Indications for removal of the uterus were not definitely obtained in every case. However, in six cases, the operation was done for myomas, and in one case, a subtotal hysterectomy was performed for carcinoma of the uterine fundus. In three cases, the hysterectomy operation was performed primarily for correction of uterine prolapse. The complaint of all of the patients when seen with vaginal prolapse, was a mass protruding from the vagina, which was more or less incapacitating. Also, dysuria and incontinence were complaints of some patients.

Table I shows the treatment given in 14 of the 16 cases. Also listed are the ages of the patients, the time of occurrence of the prolapse following the hysterectomy, and the results of the treatment given.

*Read before the Central Association of Obstetricians and Gynecologists at Louisville, Ky., on Oct. 23, 1947.

TABLE I. SIXTEEN CASES OF VAGINAL PROLAPSE FOLLOWING ABDOMINAL HYSTERECTOMY

NUMBER	AGES	OCCURRENCE OF PROLAPSE AFTER HYSTERECTOMY	TREATMENT	RESULTS
8	32-65	0-16 years	Plastic repair	7 completely satisfactory 1 partially satisfactory
4	62-68	1-15 years	Colpocleisis	Satisfactory
2	67-69	5-12 years	Pessary	Relief
2	49-67	0-10 years	None	

In five of the cases observed, there was complete eversion of the vagina. In two of these cases, repair had been previously attempted and was unsuccessful. In eight cases, the operation employed was a plastic procedure utilizing the same supportive structures and following the same operative principles which are used by many pelvic surgeons in repair of genital prolapse at the time of vaginal hysterectomy.

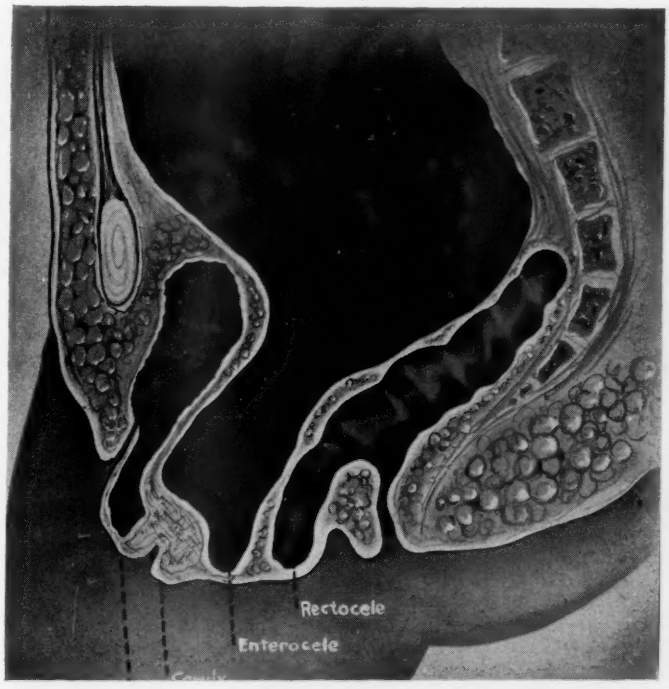


Fig. 1.—Prolapse of the vagina following subtotal hysterectomy.

Technique of Plastic Operation

The mucosa of the everted vagina is incised by a midline incision extending posteriorly from a point just below the urethral meatus and encircling the cervical stump. The vaginal mucosa with the underlying fascia is widely dissected from the bladder. The bladder is separated from the cervical stump with or without opening the peritoneal cavity anteriorly. The posterior cul-de-sac is then opened. This is usually done very readily because of the protruding enterocele. The fascial attachment of the transverse cervical (cardinal, or Mackenrodt ligaments or parametrium), and uterosacral ligaments to the stump

are clamped, cut, and ligated. The uterosacral and transverse cervical ligaments fuse at their uterine attachment and do not appear as distinct structures, but as a single fascial attachment. It is frequently not advisable to attempt to remove the entire stump because of peritoneal adhesions. But the canal with its epithelial lining can be removed, leaving the remainder of the cervix to which the ligaments are attached. A portion of the peritoneum of the enterocele between the uterosacral ligaments is removed and the overstretched uterosacral ligaments identified. These ligaments are united by chromic No. 1 interrupted sutures. These sutures are carried as high toward the promontory of the sacrum as is possible, to approximate the peritoneum and musculofascial structures without causing undue tension. This step prevents a recurrence of the enterocele of the posterior cul-de-sac.

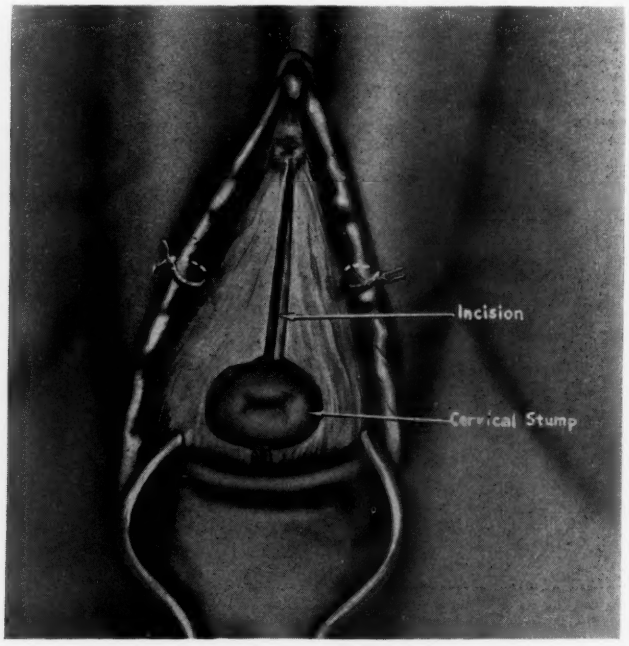


Fig. 2.—The everted vaginal wall is opened by a midline incision encircling the cervical stump.

The next suture (on a strong cutting-edge needle) is passed through the vaginal mucosa just beneath the attachment of the labia minora and carried into the periosteum of the pubis and then through the strong fascia structures lateral to the urethra. This suture then takes in the ligament stumps and passes through the sutured uterosacral ligaments, the peritoneum, and vaginal wall posteriorly. It is well to encircle the ligament stumps with a few stitches to secure hemostasis and prevent tearing out. A like suture is placed on the opposite side.

After these inclusive sutures are placed (but not tied), the fascia of the anterior vaginal wall (the pubocervical fascia), if discernible, is dissected from the vaginal wall flaps. In many of these cases, this fascia is somewhat fragmentary and cannot be sutured as a separate structure. When this is the case, all the structures in the vaginal wall are united as one layer in a single row of sutures. When the anterior vaginal fascia is adequate in amount and strength, it may be imbricated. If the patient has had urinary incontinence, the urethra

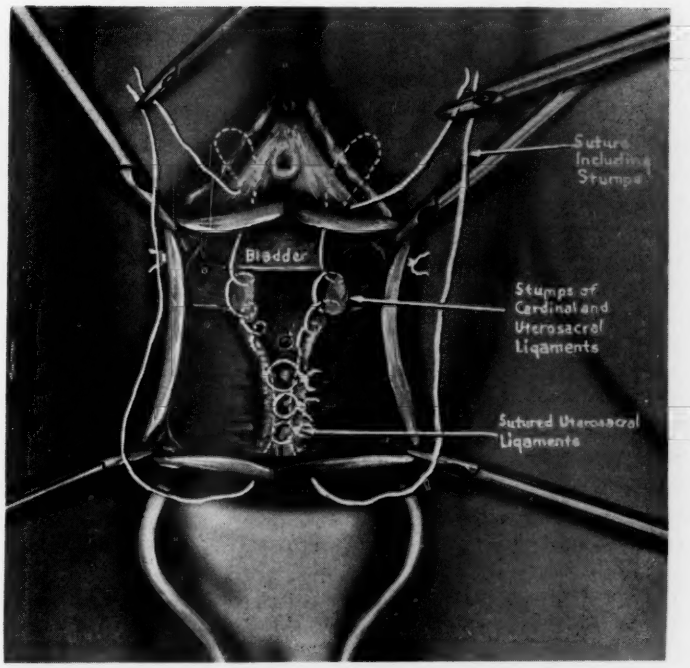


Fig. 3.—The cervical stump is removed. The fascial attachments to the stump have been ligated. The uterosacral ligaments are sutured together and a suture is passed through the vaginal wall anteriorly, the periosteum of the pubis, around the ligament stumps, and out through the posterior vaginal wall. This suture is tied after the vaginal mucosa is closed.

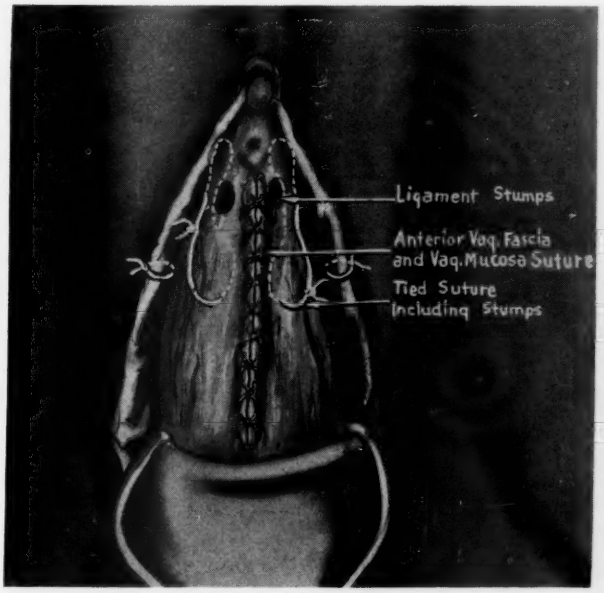


Fig. 4.—The pubocervical fascia and vaginal mucosa are sutured. The inclusive sutures attached to the fascial supportive structures are now tied.

is dissected free and a succession of mattress sutures taken, as is the usual procedure for the cure of incontinence.

The vaginal wall is sutured by interrupted sutures, before the inclusive sutures attached to the ligaments are pulled taut and tied. If the vaginal wall is sutured before the sutures attached to the ligaments are tied, more accurate approximation can be attained. This method of repair of vaginal prolapse is similar to that described by Heaney[2] and others for the correction of prolapse at the time of vaginal hysterectomy. The procedure appears to be particularly suitable for the cases of incomplete prolapse but may be inadequate for some cases of complete herniation of the vagina.

In four cases of complete vaginal prolapse in older women in whom a functioning vagina was of no concern, an occlusion operation of the Neugebauer-Le Fort type was performed. In every case, the results were very satisfactory.

In the material of this report, no abdominal operations were performed, although such procedures appear suitable for cases of complete prolapse in younger women in whom a functional vagina is desirable, especially if vaginal repair has been unsuccessfully attempted, or following complete hysterectomy, where the supporting structures appear to be inadequate for repair.

A perineorrhaphy should regularly be performed with any procedure for correction of this condition. It is important in doing the perineorrhaphy not to remove an extensive amount of vaginal wall because this will diminish the capacity of the vagina, which is unavoidably shortened by extensive plastic procedures.

Discussion

From a review of this small group of cases, it is likely that in many instances genital prolapse existed at the time the hysterectomy was performed, was unrecognized, and the operation selected was not adequate for its correction. However, this is not always the case. In some elderly patients, the loss of pelvic fat and atrophy of the pelvic supportive structures associated with advancing years permit prolapse of the vaginal vault which is not present at the time of hysterectomy. Occasionally, a large uterine tumor that cannot enter the true pelvis prevents prolapse of the uterus but, after its removal, prolapse of the cervical stump or vaginal vault occurs.

Anatomical studies of the supports of the uterus and vagina by Curtis and his associates[3-5] and studies of the mechanics of uterine support by Mengert[6] have unquestionably shown that uterine and vaginal support in the main depends upon the integrity of the derivatives of the endopelvic fascia which is attached to the lower portion of the uterus, the cervix, and upper portion of the vagina. Uterine and vaginal prolapse is always the result of injury or congenital defect of these structures. They have been confused by nomenclature, but are frequently named the paravaginal fascia, the transverse cervical, and uterosacral ligaments. The paravaginal extension of fascia is so important that the vagina does to a great extent support the cervix rather than the cervix contributing to the support of the vaginal vault.

In most instances, prolapse of the cervix or vaginal vault following removal of the uterus is preventable. Clinical experience and anatomical studies have shown that suspending the cervix or vaginal stump by the round and infundibulopelvic ligaments, which are not supporting structures, following hysterectomy is a useless procedure. Suture of the anterior and posterior

fascias of the vagina, which are extensions of the transverse cervical and uterosacral ligaments, aids in supporting the stump, but if the paravaginal fascia is intact, vaginal prolapse is not likely to occur if no attempt whatever is made to suspend the stump. If descensus is present at the time hysterectomy is contemplated, vaginal removal of the uterus and repair of the hernial defect is the procedure of choice. In cases of large uterine tumors associated with descensus, a combined vaginal and abdominal operation may be necessary.

When vaginal prolapse does occur subsequent to hysterectomy, it presents a surgical problem that is considerably more difficult than genital prolapse before the uterus has been removed.

From the number of surgical procedures which have been devised for the correction of vaginal prolapse, it is obvious that no single, or simple operation will give satisfactory results in every case. Vaginal occlusion operations have been used for uterine and vaginal prolapse for many years, but are suitable for only a limited number of patients. For elderly and noncohabitating women, it is a short and simple operation which usually gives very satisfactory results. In patients who are not good surgical risks, a partial or complete colpocleisis operation may be performed with local infiltration anesthesia. A vaginal operation has been devised by Miller[7] which attaches the vagina high in the pelvis to the uterosacral ligaments. Other procedures which attach the vagina to the anterior abdominal wall have been devised by Brady[8] and Ward,[9] using silk sutures and ox fascia lata. More recently, an abdominal operation has been employed wherein strips of rectus fascia have been attached to the vaginal stump which reinvert the vagina. Satisfactory results have been reported.

Summary

Sixteen cases of vaginal prolapse following subtotal abdominal hysterectomy were studied. Prolapse of the cervical stump occurred within from less than one year of 16 years following the hysterectomy. No cases were observed following total abdominal or vaginal hysterectomy.

The treatment in 14 cases consisted of: a vaginal plastic procedure in 8 cases; colpocleisis in 4 cases; and 2 cases were treated by wearing a pessary.

A study of the anatomy and mechanics of uterine and vaginal support and also clinical observation demonstrate that removal of the cervix with the fundus of the uterus does not predispose to prolapse of the vagina.

When uterine descensus is present at the time of hysterectomy, vaginal removal of the uterus and repair of the hernial defect will prevent subsequent prolapse of the vagina.

References

1. McKinnon, D. A., and Counseller, V. S.: Surg., Gynec. & Obst. **74**: 957, 1942.
2. Heaney, N. S.: Am. J. Surg. **68**: 284, 1940.
3. Curtis, A. H., Anson, B. J, and McVary, C. B.: Surg., Gynec. & Obst. **68**: 161, 1939.
4. Curtis, A. H., Anson, B. J., and Beaton, L. E.: Surg., Gynec. & Obst. **70**: 643, 1940.
5. Curtis, A. H., Anson, B. J., and Ashley, F. L.: Surg., Gynec. & Obst. **74**: 709, 1942.
6. Mengert, W. F.: Mechanics of Uterine Support and Position, AM. J. OBST. & GYNEC. **31**: 775, 1936.

7. Miller, Norman F.: New Method of Correcting Complete Inversion of Vagina With or Without Complete Prolapse, Two Cases, Surg., Gynec. & Obst. **44**: 550, 1927.
8. Brady, Leo: AM. J. OBST. & GYNEC. **32**: 295, 1936.
9. Ward, Grant E.: Arch. Surg. **36**: 163, 1938.

Discussion

DR. EDWARD ALLEN, Chicago.—The large number of new procedures reported in the recent literature is direct evidence of its frequent occurrence in the inadequacy of our varied techniques. A similar discussion and devising of new techniques is going on in the consideration of inguinal and femoral herniation. Many inguinal and femoral hernias are still recurring. The constitutional inadequacy of most of these individuals is well recognized. It is difficult to build a permanent water-tight dam out of secondhand lumber. Until we can build and breed more adequate structural supports into our adolescents and generally do better obstetrics, I fear we will have this problem continuously with us. Complete prolapse in the nullipara is strong circumstantial evidence to this fact.

It is very interesting that all of the patients observed by Dr. Bickel had been subjected to abdominal hysterectomy. Avoidance of this complication is one of the usual reasons given for removing the uterus through the abdomen. I should like to ask Dr. Bickel what percentage of these cases had evidence of vaginal repair other than episiotomy.

It is naturally a much more difficult procedure to secure adequate functional results in repair of a complete eversion of the vagina than it is when the herniation has occurred through a relatively small break in the fascial planes. The difficulties are increased considerably if scar tissue is present from a previous attempt at operation, although I believe some of our good results are due to causing scar tissue in the right place. The majority of the patients upon whom I have operated for this condition have had supravaginal abdominal hysterectomy without any, or with very inadequate, attempts at pelvic repair. However, this same condition existed in two patients in whom the uterus had been removed vaginally; the third patient had had the usual vaginal hysterectomy and repair. Again, this demonstrates a fact which we have all known for a long time, namely, one cannot successfully suspend the vaginal vault from above by attaching it to any of the intra-abdominal structures alone. As the author states, Curtis, Mengert and others have shown by anatomic and experimental studies the great importance of the parametrium which we call the cardinal and uterosacral ligaments and paravaginal fascia. One recognizes this fully during vaginal hysterectomy; when these structures are divided, increased mobility of even a greatly enlarged uterus immediately occurs. This increased mobility is frequently entirely inadequate to complete the hysterectomy until the vaginal canal is straightened out by depression of a high perineal body by a strong resident or Schuchardt's incision.

For many years, most of the men on our gynecologic service have, in marked prolapse or eversion, sutured the round ligament stumps high along the urethra in approximately the same position as Dr. Bickel has described. We have anchored them to the vaginal mucosa and para-urethral fascias but have not included the periosteum of the pubis. Generally the right ligament is sutured to the left angle and the left to the right, forming a sling. However, we have felt that the change in angulation produced in the vagina was more important than the building of a wall of tissue which is normally so mobile and so easily stretched. I venture a guess that the excellent results reported by Dr. Bickel were increased in part by a change in the angulation of the vagina when the posterior ligaments were drawn far forward rather than the fixation to the low level of the pubic periosteum. This drawing forward of the posterior supports should in a sense obliterate the cul-de-sac, which most of us feel is quite important in this type of repair. It is felt that this, as well as the high suture of the uterosacral ligaments, directed the downward thrust of the abdominal contents backward toward the hollow of the sacrum and strong upper levator sling rather than mere supports from the lower margin of the symphysis pubis. However, Miller, in describing his repair operation, believes that stronger high sacrouterine fixation will hold the vault of the

prolapsed vagina in its elevated position. Dr. Bickel has indicated the similarity of the placement of the fixation suture to the one usually used to close the outer corners of the incision for vaginal hysterectomy. He has also stressed the need for adequate posterior repair as a most important part of this procedure.

The vast majority of all of the patients upon whom I have operated for procidentia, and especially those in whom recurrences have happened or who have come to me for secondary repair, have been fat women, many of them with an abnormal bacterial flora in the vagina. It seems to me these factors are just as important as they have been proved in breakdown of the abdominal scar. Many of my best results in secondary repair have been in those patients in whom weight reduction, improvement in resistance, and curing infection in the vagina have preceded the operation; my poorest results when they have not been corrected. I believe the cervical stump can usually be safely and completely removed and should be on account of the risk of stump carcinoma.

DR. PAUL FLETCHER, St. Louis, Mo.—We have seen seven cases of complete prolapse of the vagina in seven years. In two of these the cervix was present, in the others removal had been complete. In each case the original operation had been done by some one other than a trained gynecologist. In all of our cases, previous attempts had been made to repair the prolapse.

I would like to ask Dr. Bickel in how many of his cases a previous attempt had been made to correct the prolapse.

DR. BICKEL (Closing).—In two of the reported cases, unsuccessful attempts at repair had previously been made; both were cases of complete vaginal prolapse. These cases might have been suitable for Dr. Fletcher's operation. It is unlikely that any of the cases reported had episiotomy and repair at the time of their deliveries.

I mentioned passing a suture through the periosteum. This is usually attempted but not always accomplished and is not essential. But in attempting to pass the suture through the periosteum, one does necessarily include the strong fascial structures lateral to the urethra which play an important part in the supporting mechanism.

TREATMENT OF URINARY TRACT INFECTIONS WITH SULFATHALIDINE (PHTHALYLSULFATHIAZOLE)*†

C. Gordon Johnson, M.D., F.A.C.S., Lee H. Lorenzen, M.D., and Ruth Y. Mayne, M.S., New Orleans, La.

(From the Department of Obstetrics and Gynecology, Tulane University of Louisiana, School of Medicine, and the Charity Hospital of Louisiana at New Orleans)

THE treatment of urinary tract infections has always been a matter of some concern. This is evidenced by the multiplicity of methods: acidification, alkalinization, urinary antiseptics, sulfonamides, and antibiotics. With the development of specific drugs, it was hoped that the treatment would no longer be a problem. This is quite true in the great majority of uncomplicated acute infections. Cook has stated that 90 per cent of such cases can be cured with one of the sulfonamides.[1] Penicillin has been of considerable help in complicated cases where most sulfonamides cannot be used safely because of toxicity or sensitivity. However, this antibiotic has failed to be of value in infections caused by the colon-typhoid group of organisms. Streptomycin has a supposed specific action on these organisms. However, it is contraindicated in pregnancy because of the possible injury to auditory and vestibular nerves.[2] There are some urinary infections that do not respond, and others that have a tendency to recur.

It is the urinary tract infections caused by *Esch. coli* that aroused our special interest. Many acute infections with this organism respond to sulfadiazine or sulfathiazole, but the chronic cases often are not affected. In complicated cases occurring during pregnancy or postoperatively, one must use these drugs with considerable caution. Thus it is necessary to find a compound which will cure urinary infections of *Esch. coli* in both acute and chronic cases and which will be sufficiently nontoxic to allow its use in cases with complications such as impaired renal function, severe anemias, pregnancy, etc.

With this in mind, Everett and his co-workers[3] studied the use of sulfasuxidine in such cases and found it to be of considerable value. This drug had been used in gastrointestinal surgery to reduce the *Esch. coli* content of the bowel. It was found by Poth and his collaborators[4, 5] at Johns Hopkins University that only 5 per cent of the drug was excreted in the urine. Blood levels were never more than 1.5 mg. per cent of sulfathiazole and 2 mg. per cent of succinylsulfathiazole (sulfasuxidine). Because of its scanty absorption and low toxicity, sulfasuxidine is well tolerated even in complicated cases. However, Poth,[5] Clay and Pickrell,[6] and Johnson[7] reported several unfavorable reactions, one of which was a case of fatal agranulocytosis. Most of the reactions were said to be due to a sensitivity or idiosyncrasy to sulfathiazole. Everett[3] stated that his chief objection to the drug was its expense due to the large dosage required.

*The Sulfathalidine used in this study and funds for this study were supplied by Sharp & Dohme, Inc.

†Read before the Central Association of Obstetricians and Gynecologists in Louisville, Ky., on Oct. 25, 1947.

Everett advances two theories as explanation for the cure of urinary infections by this scantily absorbed drug. Succinylsulfathiazole itself has little "in vitro" value. However, some of the drug hydrolyzes in the body to succinyl acid and sulfathiazole or other similar compounds. Either this small amount of free or "split" drug excreted in the urine is enough to render it sterile or else the tissues of the urinary tract are allowed to rid themselves of infection when the source of contamination in the bowel is temporarily eliminated.

Sulfathalidine (phthalylsulfathiazole), like sulfasuxidine, is a member of the N^4-carboxyacyl-sulfathiazole family. It has also been found to act in vivo in a manner similar to sulfasuxidine. About 90 to 95 per cent of the drug remains in the gastrointestinal tract. Poth and Ross[8] found that in a dog receiving 0.5 Gm. per kilogram per day, the bacterial count fell from 10,000,000 to less than 10 per Gm. of wet stool in six days. As indicated by the alteration of the coliform flora in the bowel of man, phthalylsulfathiazole, in half the dosage, is as effective as succinylsulfathiazole.[9] Poth also found that the maximum concentration of the conjugated drug (phthalylsulfathiazole) in the blood, with a dose of 1.0 Gm. per kilogram of body weight per day, has not exceeded 3.3 mg. per cent. Streicher[10] has found that, irrespective of the dose, the concentration of sulfathalidine in the blood stream of human beings ranges from 0.5 to 1.5 mg. per cent. Poth and Ross[9] report that approximately 5 per cent of the orally administered therapeutic dose is excreted in the urine. Crystals have not been observed following oral administration of the drug. This is due to the fact that the free form is not excreted in large quantities and because the conjugated drug forms soluble salts even at a pH of 5.6. Thus it may be seen that high bacteriostatic concentrations are readily produced and maintained within the bowel, that blood levels are clinically insignificant, and that drug crystalluria or renal obstruction has not been observed.

Poth and Ross[8] reported that no toxic reactions had been demonstrated in dogs receiving oral doses of the drug. Intravenous injections caused vomiting at first but did not occur on further injections. There have been few toxic reactions seen in human beings. The same authors[9] reported headache, nausea without vomiting, and fever in one woman who had developed the same reaction to sulfasuxidine. She was obviously sensitive to sulfonamides. These workers warn that as more persons receive the drug, it can be expected that more toxic manifestations will be seen; however, such reactions will be relatively infrequent.

Methods and Results of Study

The patients reported herein were those having a urinary infection as a complication of some gynecologic surgical procedure or of pregnancy. The diagnosis, initially made from signs and symptoms and by microscopic examination of a catheterized specimen of urine, was confirmed by culture.

The first culture was made before therapy was begun. In most cases, cultures were repeated at the end of the first week's treatment and subsequently every week until negative. Additional cultures were made every second week for several months.

Cultures were managed as follows: After centrifugation of the specimen, the sediment was streaked on a heart infusion agar with 1 per cent filtered lactose and an indicator of bromthymol blue. For the growth of anaerobes, particularly streptococci, two loopfuls of sediment were inoculated into recently heated thioglycollate broth with methylene blue indicator. All organisms which grew during incubation of these media at 37 degrees for two days were identified.

There were a total of 47 cases treated with sulfathalidine. *Esch. coli* was the organism involved in 27 cases. Four of these had mixed infections. The

other twenty cases had various other bacterial invaders. The types of cases with *Esch. coli* infections, along with the immediate results of treatment, are noted in Table I.

TABLE I. TWENTY-SEVEN CASES WITH URINARY INFECTIONS OF ESCH. COLI TREATED WITH SULFATHALIDINE

CASES ASSOCIATED WITH	PYELITIS		CYSTITIS		TOTAL	IMMEDIATE RESULTS AFTER TREATMENT	
	ACUTE	CHRONIC	ACUTE	CHRONIC		SYMP. CURE	BACT. CURE
Pregnancy	2	4	9	0	15	13	12
Gynecological Conditions	0	0	8	4	12	14	14
Total	2	4	17	4	27	27	26

The majority of the cases were treated with sulfathalidine for one to two weeks. However, since five persons did not return as directed, more drug was given because of the interruption of treatment. Four of the latter had three weeks' treatment and the fifth, four weeks. The routine of treatment was 6 Gm. per day, divided into 6 equal doses every four hours, for the time of hospitalization (approximately one week), and 4 Gm. daily for the ensuing time. Eight cases, two of which had chronic infections, were treated with 2 or 3 Gm. daily. There was no difference in the response of this latter group and that of the group treated with a larger amount of drug.

No patient received more than 6 Gm. daily, or approximately 0.1 Gm. per kilogram of body weight. The total amount of drug given to each patient varied from 27 to 86 Gm.; however, most of the patients received 42 to 72 Gm., or an average of 53 Gm. This compares very favorably with the amount of succinylsulfathiazole necessary to obtain comparable results. Everett used 0.25 Gm. of succinylsulfathiazole per kilogram per day for one week and another 0.125 Gm. per kilogram for one to two additional weeks. For a person of 60 kg., this is probably a total dosage of 157 to 210 Gm. of sulfasuxidine, or approximately three and one-half times the total dose of sulfathalidine.

The first culture taken after treatment of each case of *Esch. coli* was negative. After treatment was begun, negative cultures were obtained in fourteen or 50 per cent within the first week, and seven or 27 per cent within the second week, an over-all total of 21 or 77 per cent within two weeks or less. Unfortunately, some of the patients were discharged from the hospital in a very short time, so that in thirteen cases or approximately 50 per cent, including the above-mentioned seven or 27 per cent, the first control culture was taken later than one week after treatment. Also, since most of the patients were treated in the clinic, it was not practical to obtain cultures other than at weekly intervals. In one case, the specimen contained *Esch. coli* after the second week of treatment. This occurred just before delivery in a patient having ureteral block; however, with no additional treatment, there was a negative culture after delivery two months later. After two weeks' rest from the drug, another patient had a recurrence which was cured permanently with ten days of treatment.

There were four mixed infections of *Esch. coli* and *Staphylococcus albus* or an enterococcus, all of which were cured of the bacilli with sulfathalidine. One of the cases of staphylococcus infections cleared without additional treatment and the other was cured with penicillin. The enterococci were eradicated with mandelic acid but reinfections occurred.

Table II shows the number of cases which were observed for varied periods. It may be seen that eight cases, followed for two months, and fourteen cases, followed for three months to one year after the time of treatment, were cured symptomatically and bacteriologically.

TABLE II. TIME CASES WERE FOLLOWED AFTER TREATMENT

TIME	BACTERIOLOGIC AND SYMPTOMATIC CURES	INCOMPLETE TREATMENT	REINFECTIONS
2 months	8		
3 months	3		1
4 months	2	1	
5 months	2		
6 months	4		
7 months	1		
8 months	1		
1 year	1		
Immediate cure but no follow-up after treatment	3		
Total	25	1	1

There was only one case of reinfection with *Esch. coli.* This appeared three months after the original treatment. However, there were four cases of reinfections with other organisms after the *Esch. coli* was eliminated. Three of these were *Aerobacter aerogenes* and one was *Alkaligenes fecalis.*

Case Reports

Mrs. F. L., aged 24 years. This patient developed acute cystitis after an abdominal hysterectomy in December, 1944. She was known to have a right ureteral stricture and was under the care of a urologist prior to surgery. Cultures taken in the hospital were positive for *Esch. coli.* The patient was known to be quite sensitive to sulfathiazole and was given sulfacetamide with poor results. Mandelic acid was also tried but not successfully. On Jan. 3, 1945, she was given 2 Gm. sulfathalidine for the first dose, and 2 Gm. daily thereafter for fourteen days. On January 9th, six days later, the urine was free from pus cells, and the patient was symptomatically cured. No further trouble took place. Subsequent urine cultures were negative for *Esch. coli.*

Miss B. F., aged 40 years. This patient had a chronic pyelo-cystitis, which began in October, 1945. Cultures were positive for *Esch. coli* at this time. The patient was treated by a urologist in October and November, 1945, with sulfacetamide, but with poor results. In January and February, 1946, she had severe right kidney pain and was treated with penicillin, but the urine continued to contain pus and *Esch. coli* organisms. In March, 1946, the urine showed many pus cells and the pain in the right kidney region returned. In April, 1946, when there was a recurrence of pain and positive cultures, the patient was put on mandelic acid by the urologist, but again the results of treatment were poor. On Dec. 16, 1946, the patient had another recurrence of kidney infection with a positive culture for *Esch. coli.* At this time she was put on sulfathalidine, 2 Gm. immediately and 2 Gm. daily for fourteen days. On December 19th, three days later, symptoms were much improved and there was a marked decrease in the number of pus cells in the urine. On December 23rd, there were very few pus cells, and on February 13th, the urine culture was sterile. It was sterile also on March 6, 1947. Since the recrudescence in December, 1946, there has been no return of symptoms. The last urine culture on August 6th, eight months after treatment, was negative.

It has been mentioned that 20 other cases of various types of infections were treated. The same routine of treatment was used for these as for the patients having *Esch. coli* infections. Table III shows the results of treatment of these cases.

TABLE III. URINARY INFECTIONS WITH ORGANISMS OTHER THAN ESCH. COLI

ORGANISM	TYPE OF INFECTIONS					
	ACUTE			CHRONIC		
	NO. CASES	SYMP. CURES	BACT. CURES	NO. CASES	SYMP. CURES	BACT. CURES
Staphylococcus	5	5	5			
Streptococcus	3	3	2			
Aerobacter aerogenes	1	1	1	4	0	0
Alkaligenes				2	2	0
Mixed	4	4	3	1	1	1
Total	13	13	11	7	3	1

The acute cases due to staphylococci or streptococci were cured of their infection but the chronic ones were not. There was a striking failure of the drug to influence the condition in cases infected with *Aerobacter aerogenes* and *Alkaligenes fecalis*. This was also noted by Everett in his work on sulfasuxidine. Nevertheless, all cases except four which were infected with *A. aerogenes* improved symptomatically.

As a control of the drug, seven cases of *Esch. coli* and seven other infections were treated with sulfadiazine. The sulfadiazine was given only while the patients were at the hospital; so treatment varied from three to fourteen days. All cases of colon infections were acute and were cured. Of the other infections, two acute cases of staphylococcus and streptococcus were cured, one paracolon pyelitis was cured temporarily, but four cases of *A. aerogenes* or *Alk. fecalis* were not cleared of their infections. Three of these failures were improved symptomatically, however.

None of the patients showed evidence of toxicity or reaction from the sulfathalidine. One patient had been given four weeks' continuous treatment with sulfathalidine in a test of the value of the drug against enterococcus infection. After a month's rest, she was given another two weeks' treatment. There was no sign or symptom of toxicity with this long treatment. Another case had had the left kidney removed and now had pyelitis of the right kidney. This person received treatment for thirteen days when she began to vomit following ingestion of the medicine. She was later treated for seven days without any untoward reaction. It was very questionable that the medication was the cause of her nausea.

Discussion

Most uncomplicated, acute, urinary tract infections can be controlled by use of the sulfonamides. However, chronic cases, especially those due to *Esch. coli,* often resist all forms of therapy. With sulfathalidine, we have been able to cure both acute and chronic urinary tract infections due to colon organism. Even where there was a mixture of organisms, the colon bacilli were eradicated. The effectiveness of the drug is made evident by the short time necessary to obtain negative cultures and by the long period of negative cultures after cessation of treatment. The prompt cure of chronic cases which had previously resisted other therapy also attests to the value of sulfathalidine in *Esch. coli* urinary tract infections.

It was interesting to find that five cases of acute staphylococcal cystitis and two of three cases of acute streptococcal cystitis were cured symptomatically and bacteriologically with sulfathalidine.

It was also noted that, like sulfasuxidine, the drug had little effect on urinary tract infections due to *Aerobacter aerogenes* and *Alkaligenes fecalis.*

We agree with Everett that the most probable mode of action of both sulfasuxidine and sulfathalidine is twofold. The elimination of the foci of infection in the bowel apparently gives the urinary tract tissues time to combat the infection through their own resistance; moreover, the "beneficial effect exerted on the intestinal tract may decrease the avenues of escape of organisms into the blood stream or lymphatic channels through which they may have been reaching the urinary tract." We also feel, however, that there is some definite sensitivity of *Esch. coli* organisms to this particular type of sulfonamide or to its products in the body.

As in the case of sulfasuxidine, the lack of toxicity of sulfathalidine is a factor which allows treatment in conditions such as impaired renal function and severe anemias. These conditions are often found during pregnancy, and ordinary sulfonamides would be contraindicated.

With sulfathalidine there was not the objection of high cost of the drug due to large amounts required, as found by Everett. Whereas he found it necessary to use an average of 0.25 Gm. of sulfasuxidine per kilogram daily for one week and half this amount daily for a second week, we were able to accomplish similar results with an average dose of 0.1 Gm. thalidine per kilogram daily for one to two weeks. In eight cases, a smaller dose, 0.05 Gm. per kilogram, was used with excellent results.

As is expected with acute infections, average doses of sulfadiazine gave good results in seven cases of acute cystitis caused by *Esch. coli.* However, four cases of *A. aerogenes* and *Alk. fecalis* infections failed to respond to this drug.

Streptomycin has been reported as being efficacious for *Esch. coli,* but there have also been reports of auditory and vestibular nerve injuries from this antibiotic. Therefore, we would be hesitant to use streptomycin during pregnancy and recommend sulfathalidine as the therapeutic agent of choice.

Summary and Conclusions

1. We have used phthalylsulfathiazole successfully in the treatment of acute and chronic urinary tract infections due to *Esch. coli.*

2. Chronic cases of *Esch. coli* that were resistant to other sulfonamides, penicillin, and mandelic acid were cured bacteriologically with sulfathalidine.

3. Twenty-six out of twenty-seven cases of *Esch. coli* infections were cured symptomatically and bacteriologically.

4. Negative cultures were obtained in 50 per cent of the cases in one week or less and in 77 per cent in two weeks or less.

5. The first culture taken after treatment (which, in twelve cases, was after the first week) was negative in all cases.

6. Sulfathalidine did not seem to have any effect on cystitis caused by *Aerobacter aerogenes* or *Alkaligenes fecalis.* It did have some effect on urinary tract infections caused by staphylococci and streptococci.

7. Sulfathalidine can be used where other sulfonamides would be contraindicated because of its poor absorption and low toxicity. This is especially true in pregnancies complicated by impaired kidney function or severe anemia.

8. The dosage necessary to bring about a cure was 0.1 Gm. per kilogram of body weight daily for an average of two weeks. Eight cases were given 0.05 Gm. per kilo.

9. Due to the low dosage required, the cost of the drug does not make its use prohibitive in the low income group.

10. Its mode of action is most probably similar to that advanced by Everett and his co-workers for sulfasuxidine.

References

1. Cook, E. N., quoted by Payne, F. L. in discussion of No. 3.
2. McDermott, Walsh: Am. J. Med. **2**: 491-500, 1947.
3. Everett, Houston S., Scott, Roger B., and Steptoe, Philip P.: Am. J. Obst. & Gynec. **49**: 114-127, 1945.
4. Poth, E. J.: J. A. M. A. **120**: 265, 1942.
5. Poth, E. J., and Knotts, F. L.: Arch. Surg. **44**: 208, 1942.
6. Clay, R. C., and Pickrell, K. L.: J. A. M. A. **123**: 203, 1943.
7. Johnson, S. A. M.: J. A. M. A. **122**: 668, 1943.
8. Poth, E. J., and Ross, C. A.: Texas Rep. Biol. & Med. **1**: 345-370, 1943.
9. Poth, E. J., and Ross, C. A.: J. Lab. & Clin. Med. **29**: 785-808, 1944.
10. Streicher, M. H.: J. A. M. A. **129**: 1080-1082, 1945.

POSTMATURITY*

L. A. Calkins, M.D., Ph.D., Kansas City, Kan.
(From the Kansas University Medical Center)

MANY years ago, Dr. Rudolph Holmes stated that there was no problem in postmaturity. Textbooks continue to suggest, however, that labor may be more difficult in patients going well past their due date by virtue of the increased size of the baby and the lessened possibility of molding of the more ossified head. Williams and others have, however, consistently advised against induction of labor in order to avoid these possible difficulties.

As far as we have been able to determine from the literature, no one has ever accurately proved that postmature babies are larger, and if so, by how much. Nor has anyone actually determined, except in isolated case reports, that the postmature heads are less well molded in the birth process.

In a recent rather careful study of the size of placentas at the various stages of pregnancy and the correlation of placenta size with infant size, some very interesting data were developed. It was found that the growth curve for both placentas and babies follows the general form of the elongated S so characteristic of all mammalian growth. Increase in size continues throughout the pregnancy, but contrary to the impression given by the Hasse formula and other estimates of growth (except the Scammon-Calkins formula), this growth is not at a uniform rate. In the case of the placenta weight and the baby weight, growth is rapid up to about the two hundred sixtieth day. It is much less rapid from the two hundred sixtieth to the two hundred eightieth day, and the increment after full term is reached is very small (Figs. 1 and 2).

If one divides the material into three groups, according to whether the placenta weighs less than 500 grams at the time the baby is born (wet weights), from 500 to 695 grams, or 700 grams and above, some very interesting results are obtained. The average weight of primiparous babies with small placentas at full term (270 to 289 days) is 2,810 grams. With placentas between 500 and 695 grams, the baby weight is 3,295 grams; with large placentas it is 3,675 grams. Thus the span between small and large placentas is *on the average* 865 grams. Compared with this, the increment between 280 days and 300 days is only 120 grams or less. Similar figures for multiparas are as follows:

PLACENTA SIZE	DAYS GESTATION	SIZE OF BABY
Under 500 grams	270 to 289	2875 grams
500 to 695 grams	270 to 289	3310 grams
700 grams and over	270 to 289	3795 grams

Here the difference in baby size between small and large placentas is 920 grams.

*Read before the Central Association of Obstetricians and Gynecologists, Oct. 23, 1947, Louisville, Ky.

The increment between 280 and 300 days is about 130 grams. Thus it would seem that placenta size is more significant in determining the size of the baby than is postmaturity of some three weeks' duration in the proportion of about 7 to 1.

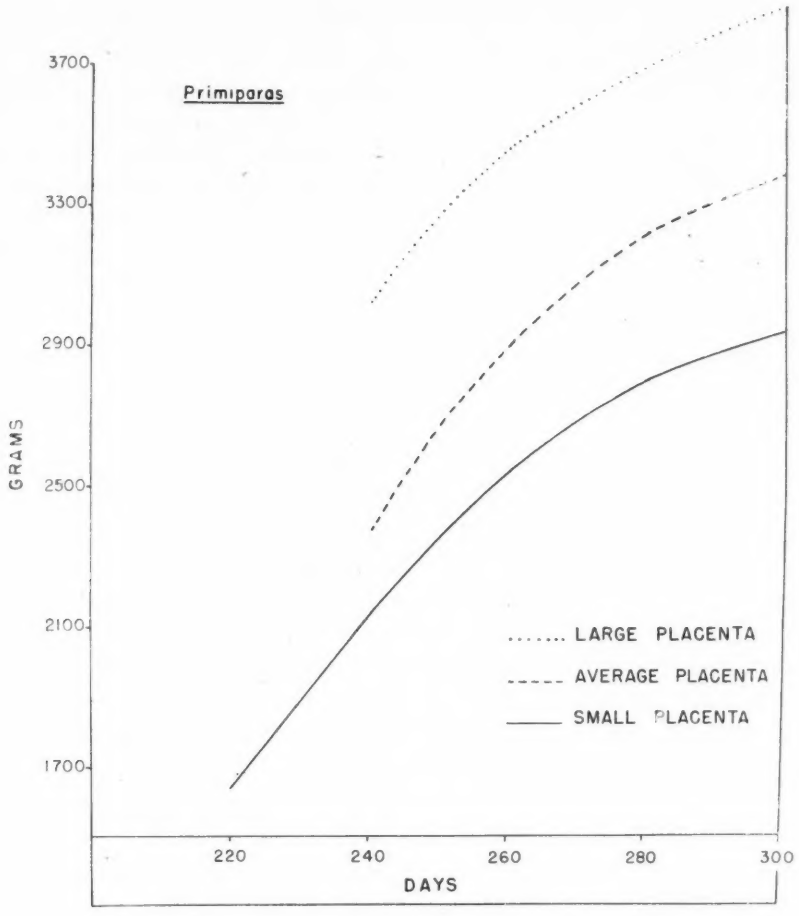


Fig. 1.

Even more striking is the fact that in the primiparas, eight patients whose pregnancy exceeded 295 days and whose placentas weighed 400 grams or less had infants not exceeding 3,000 grams in weight. On the other hand, in nine patients with a pregnancy of 264 days or less and with placentas weighing 700 grams or more the *average* weight of the baby was 3,560 grams.

From the foregoing, it is quite apparent that if an infant is to be oversize at full term, it will have acquired most of that excessive size by about the two hundred sixtieth day of the pregnancy. It is, therefore, important in those patients where the size of the infant may be a complication to recognize that large size early. On the other hand, if the infant is large at full term, its further increment in size thereafter will be so little that it will make no real

difference in the course of the subsequent labor. The obvious disadvantages of inducing labor in the presence of an unprepared cervix cannot possibly be justified on the basis of this small increment in the postmature baby.

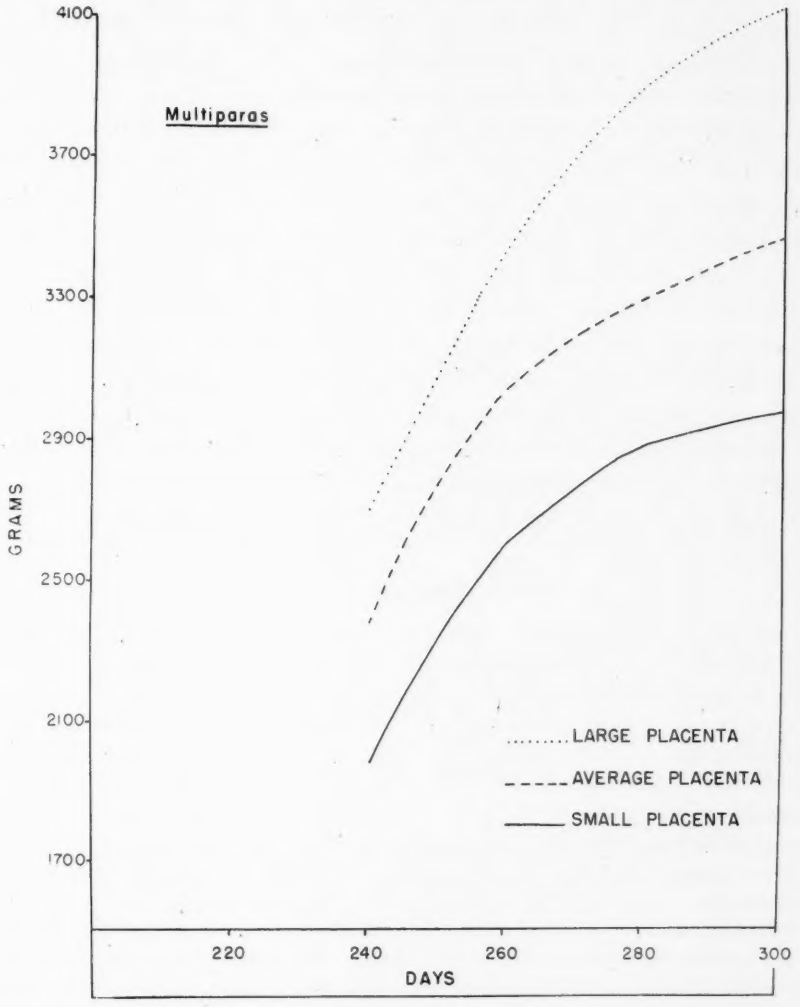


Fig. 2.

We have pointed out in a previous publication that the first stage of labor is no longer with large babies than it is with small ones. We have also pointed out that the second stage of labor in primiparas is slightly longer (by about six minutes on the average) where the baby is large. More recent, and as yet unpublished studies, would indicate that this small difference is physiologic rather than antomic in nature. It seems that the labor pains in the second stage have a tendency to be poorer with the large babies. Perhaps this is just as well. The additional six minutes (and the two or three extra labor pains involved) may produce less trauma to the birth canal and less frequent injury to the child.

I, along with many, many others, have been guilty in the past of using low forceps much more commonly with the large babies than with the small because it was felt that the second stage "would be prolonged." Unduly prolonged second stage will occur in the presence of a large baby and poor pains, but only in 5 per cent or less of patients who are not too heavily medicated, and thus cannot be offered as a reason for doing forceps deliveries on 50 per cent or more of all primiparas, more than half of whose babies will be small.

There is no doubt that ossification is going forward in the latter part of pregnancy and that this process continues after delivery. Rather extensive studies of the closure rate of both suture lines and fontanels throughout the period of infancy and early childhood are now available. Obviously a baby born as much as two months postmaturely would have some definite increase in the rigidity of its cranial vault. In this present series of 6,000 cases, there was only one patient whose pregnancy exceeded 316 days, and the vast majority of the "postmature" group were delivered at the end of 305 days or less. Thus the problem is one of two or three weeks' postmaturity, not one of two or three months. In this two or three weeks the amount of increased ossification is certainly negligible so far as creating a problem for the average patient.

It would seem safe to agree with Dr. Rudolph Holmes that there is no postmaturity problem.

Discussion

DR. GEORGE KAMPERMAN, Detroit, Mich.—This presentation on postmaturity has not in any way changed my conception or reasoning on the problem, for my attitude toward this question quite corresponds with that of the essayist.

Dr. Calkins begins his presentation with an assertion by Rudolph Holmes and ends it with an endorsement of that same opinion. In his discussion he presents research data to uphold the contention that the size of a baby depends on the size of the placenta, rather than on a short period of postmaturity.

My recent encounter with the postmaturity question has been as an executive in a very active obstetric division. As such it was always my attitude to watch over the type of obstetrics practiced and especially to try to throw influence against any too radical type of procedure. I was impressed by the fact that cases of postmaturity caused no worry and presented no problem to most of the staff members. It seemed that the indication to induce labor in cases of delayed labor was present in the practice of only a couple of men. It seemed strange that this should occur thus, and I often wondered whether so-called postmaturity was not a state of mind of the obstetrician rather than an actual occurrence.

This problem came to a head somewhat during World War II when scarcity of hospital beds resulted in a rule that the hospital could furnish no beds for patients who were not actually in labor unless some recognized complication existed. This at once put an end to the induction of labor for postmaturity, much to the relief of the entire staff and especially to those who had been accustomed to inducing labor for this indication. One does not need a great experience with attempted induction in cases of postmaturity to learn soon that it is much easier and simpler to allow patients to go into labor spontaneously than to induce labor and have to be on call rather closely during the period of induction—at times quite a prolonged period.

We might ask the question, Is there such a condition as postmaturity? Obstetric literature is rather deficient in discussions on this subject. It probably means that in most clinics

the problem is not considered important enough to deserve much study. Rathbun, in 1943, discussed the problem as it occurred in the Boston Lying-in Hospital. He classes as postmature those pregnancies where labor does not occur before 295 days after the first day of the last menses. This allows 15 days beyond what is usually considered the estimated date of delivery. In his 250 cases the statistics do seem to show a somewhat larger baby if the pregnancy goes overtime, a slight lengthening of labor, and a slight increase of interference necessary in delivery, especially of the more major types of interference. Analyses showed no increased fetal mortality that could be accredited to postmaturity. There was no increase in intrauterine fetal deaths. Masters and Clayton, reporting from England, revealed that in cases of postmaturity there was no more excessive calcification or degeneration of the placenta than in normal mature cases. They found nothing in placental study to lead one to think that intrauterine death had any relationship to postmaturity.

We might infer from Rathbun's report that there is such a condition as postmaturity. However, the series is small. What is lacking in the literature is a reported series large enough to give conclusive and convincing deductions. We have all seen so-called overdue patients with large babies but also some with small babies, and both observations hold true for patients not overdue.

But even though one might admit that postmaturity is occasionally genuine, yet it seems doubtful that it ever presents much of a problem.

Strangely enough, statistics seem to show that if a baby goes postmature beyond twenty days it begins to lose weight. So then if we estimate that prematurity does not exist until the pregnancy goes 15 days beyond the estimated date and then if the baby will begin to decrease in weight five days later, there should be little worry about excessive gain in the baby's weight. Statistically the longer postmaturity continues after twenty days, the smaller will be the baby. Furthermore, the baby's gain in weight, if it does occur, is mostly a gain in weight of soft tissues, and unless this is extremely excessive, it hardly seems it could cause much dystocia.

In conclusion we might say that although occasionally pregnancies seem to go overtime, this rarely produces a serious problem and rarely warrants drastic measures. Individualization should be the keynote and then only an occasional case will present a problem. Patients should be taught that postmaturity is rarely a problem and their anxious demands for induction of labor should be met with reassuring reasoning.

DR. P. B. RUSSELL, Memphis, Tenn.—I think one factor which is sometimes overlooked by the practitioner as well as by some of us who are specialists is the question of when quickening occurs. Sometimes this has bearing upon the medicolegal aspect of a contested paternity case. I feel the patient should return once a week from the estimated sixteenth week until the physician can hear the feal heart tones, or fetal movements, and then a date for the confinement can be estimated at this time. Menstrual history is very unreliable in many cases. I think too many of us take the first day of the last menstrual period and then estimate the confinement from this date.

DR. RUDOLPH W. HOLMES, Charlottesville, Va.—It is a popular mot that women's first babies are often prematurely born, though the infants are of average weight and lustiness, for gossipy women will reckon from the marriage day. The literature is filled with spurious contributions on postmaturity, and I know that many practitioners have them galore, but I never have seen an authenticated case. If we imagine prolongation of pregnancy is possible, the vitally important criteria must all be indubitably evaluated—the date of the last menstruation, the date of conception, the progressive rate of uterine growth, the time of perception of fetal movements by the mother, corroborated by the physician, and the day of elicitation of the fetal heart beats (and this means an almost daily auscultation during the range when conductivity will serve its purpose). All these factors are subject to evident errors. In my opinion postmaturity is a figment of the imagination.

DR. JACOB L. BUBIS, Cleveland, Ohio.—In contradiction to Dr. Holmes, there is such a thing as postmaturity. I want to report the case of a woman, aged 37 years, who had two children aged 7 and 6 years. On April 14, 1946, I performed a dilatation and curettage, perineorrhaphy, and hemorrhoidectomy on this patient. Three months later she had an attack of appendicitis which cleared up. I next saw her on Jan. 22, 1947. Her last menstrual period had occurred on December 9, and examination showed the uterus three fingers above the pubis. Her expected due date was Sept. 16, 1947. The patient reported to me regularly. At the time of her due date I did not want to aggravate the appendicitis by giving castor oil, so I let her continue. On October 14 she went into spontaneous labor and had a baby of moderate size; the cord was small and very thin and almost pulseless, and the skin was peeling from the hands, head, and body. The baby cried spontaneously but weakly. It was apathetic for several days. Since then the skin has healed completely; he takes his nourishment well and has gained in weight. However, the muscles of the arms and legs are weak and the pediatrician states that the infant has symptoms suggesting myasthenia gravis. I am quite sure this is a case of postmaturity for the records.

DR. CHARLES GALLOWAY, Evanston, Ill.—I would like to ask the essayist a question because I do not know the answer and maybe some of the others do not know it either. What about death and overdue babies? What about the patient who goes three or four weeks beyond the calculated due date and then one day shows up without fetal heart tones, or goes into labor and the baby dies during labor without any cause that one can find? Does that condition exist?

DR. CALKINS (Closing).—I always forget to give certain points in my presentations. These 6,000 patients included in this series were in a sense selected patients in that the whole series comprised something like 9,000 cases, and in 3,000 the histories of the last menstrual period were not considered sufficiently accurate. Those were, therefore, thrown out. We thought the histories in these 6,000 cases could be depended upon as being reasonably accurate and that any individual inaccuracies would be overcome by the fact that part of them would be in one direction and part in the other and would be compensatory. I am well aware of the fact that menstrual histories cannot be depended upon, but I am also quite certain that in some of the patients they can be depended upon. In a good many of these particular patients we know the histories are accurate because we saw the patients in the first month or six weeks of pregnancy and know there could be no serious inaccuracy.

Dr. Galloway has raised a question. I do not think any of us know the complete answer. We have seen this type of thing and there was one such baby in this series. However, during that same period of time we had six or eight similar stillborn babies in women delivered at full term or before full term. Dr. Galloway described a situation in which he cannot accurately ascertain the cause of fetal death, and we have had several similar patients in which this occurs in the premature group.

Dr. Kamperman made reference to the fact that the baby may get smaller if it gets sufficiently postmature. That seems hardly likely and does not obey any of the rules of growth. We noted in this series that postmaturity was much more frequent when the placenta was small and much less frequent when the placenta was large. It would, therefore, naturally follow that if one should get the weights and pay no attention to the placenta, he would get a large percentage of small babies in the postmature group and would thereby have the average postmature baby's weight reduced.

THE SURGICAL MANAGEMENT OF INCOMPLETE ABORTION*

WALTER S. MORSE, M.D., SC.D., F.A.C.S., HOUSTON, TEXAS
(From the Department of Obstetrics, Baylor Medical College)

THE abortion problem as a whole is one of increasing importance since it is directly responsible for an alarmingly high maternal mortality rate. Of the 25,938 maternal deaths in the United States which occurred in the three-year period, 1939 through 1941, nineteen per cent were directly due to abortion.[1] During 1942 there were 7,956 maternal deaths in the United States, of which 1,384 were directly attributed to abortion. Infection was by far the leading cause of death in these reports.[1] Although during 1944 the national maternal mortality rate reached a record low of 6,369 deaths, 36 per cent were caused by puerperal infection.[2] Two-thirds of the deaths following abortion, both in 1943 and in 1944, were attributed to infection.[2]

Less tangible is the permanent damage produced in the female generative tract resulting directly or indirectly from abortion.

Management of incomplete noninfected or infected abortion presents one of the most difficult problems with which the obstetrician or gynecologist must deal. The treatment usually resolves itself into some modification of one of two methods—conservative or surgical. Briefly, the conservative method consists of supportive measures, complete bed rest and the administration of oxytocics in an attempt to influence the uterus to empty itself without instrumental aid.[3-6] In a large and representative series of cases where conservative management was used, the average duration of symptoms before completion of the abortion was four weeks and four days.[7, 8]

The surgical method combines all the features of conservative management and, in addition, the uterus is emptied by instrumentation, provided the patient's condition is such that she does not constitute a poor surgical and anesthetic risk. Advocates of this procedure have shown that uterine involution is more rapid, and normal menstrual rhythm is established more quickly after surgical completion of the abortion, while the period of hospitalization is much shorter.[9-13] Patients cared for in this manner show low morbidity, and mortality rates which compare favorably with those of the more conservative management.[9, 12]

However, this method is not without danger, since it is difficult, if not at times impossible, to distinguish between infected and noninfected incomplete abortion. Due to absorption of toxic products from necrotic retained secundines, the so-called noninfected case may exhibit many clinical features resembling the infected case.[14] The uncertainty involved in choosing the proper cases for surgical management constitutes a weak feature.

*Read before the Central Association of Obstetricians and Gynecologists at Louisville, Ky., on Oct. 23, 1947.

There is probably no phase of infection as generally misunderstood as postabortal sepsis. An understanding of the process of inflammation as it pertains to the special problems of infected and noninfected incomplete abortion aids considerably in the intelligent handling of these cases. There is often a toxemia produced by the absorption of toxins resulting from necrosis of retained placental fragments. Any of the infecting organisms, singly or in combination, may be found in the postabortal uterus in all cases after the first 24 hours.[15]

Fundamentally, there are two general types of infection involved in incomplete abortion: the noninvasive and the invasive infections.[16] The noninvasive infections are usually limited to the mucosal surface and are produced predominately by the saprophytic group of bacterial organisms. The pyogenic cocci constitute the group responsible for the invasive type of infection.[17]

The early activities of the saprophytic organisms are largely limited to necrotic tissue, and the toxemia accompanying such infections is due to the absorption of degradation products resulting from chemical changes and bacterial activity in the necrotic tissue remnants.[16] The anaerobic streptococci group is made up of a large number of strains and is probably more than an occasional constituent of the normal vaginal flora.[17-20] These organisms find conditions favorable to them in the necrotic tissue of the incompletely evacuated uterus,[21] are responsible for many of the toxic symptoms,[22] and are frequently associated with the occurrence of suppurative thrombophlebitis in the pelvic veins.[23, 24]

Invasive infections differ from the noninvasive infections principally in that the organisms involved spread by the way of tissue spaces and lymphatics instead of along the surface.[12, 15, 16, 25] The essential feature is an invasion of the cocci beyond the so-called protective leucocytic zone. It is this type of infection that favors a poor prognosis.

The organisms found most constantly in the critical and fatal cases of infected incomplete abortion are the beta hemolytic streptococci.[26] Consequently, cervical or uterine cultures containing beta hemolytic streptococci have indicated that instrumental interference may aid this invasive group of organisms. This factor excluded a large group of patients from active treatment.

Lancefield and her associates,[27-30] by means of a precipitin reaction employing "C" carbohydrate antigens, isolated many varieties of beta hemolytic streptococci, of which only a relatively few strains were found to be extremely invasive in the human body. Therefore, the ability of streptococci to hemolyze blood agar media is in itself no longer a suitable criterion of invasivemess.[31] The most invasive, and consequently the variety most often associated with a poor prognosis, were placed in Group A. The less invasive beta hemolytic streptococci, and thus less often associated with a poor prognosis, were placed in Groups B, C, D, E, F, G, H, and K. Hemolytic streptococci of Group A variety are very rarely, if ever, present in the bacterial flora of the female genital tract.[23] This explains why, in the past, hemolytic streptococci have been isolated from the cervix and uterine cavity in cases of genital tract sepsis; some cases were critically ill, and others scarcely so at all.[32] The presence of Group A organisms, and not the entire group of beta hemolytic streptococci, in uterine cultures, should thus temporarily contraindicate active treatment in cases of infected incomplete abortion.

With the advent of the sulfonamide group of drugs and later, penicillin, it was believed that a panacea had been discovered for all infections; consequently, the active surgical management of septic abortion was believed to be unnecessary. However, with the general use of the sulfonamide drugs since

1937 and, more recently, penicillin, the national mortality percentages resulting from postabortal infection have been reduced little.[1, 2, 33]

Sulfonamide inhibitors have been demonstrated in necrotic tissue.[34] The sulfonamide inhibitors, the most important of which is para-aminobenzoic acid,[35-37] are bound up in the tissue proteins and are not capable of inhibiting the action of the sulfonamides until released through the necrotic breakdown of proteins[34, 38]; hence, the relative ineffectiveness of the sulfonamide drugs in combating the saprophytic type of infection. Furthermore, the anaerobic streptococci are very sulfonamide[39] and penicillin resistant.[40]

Recent clinical reports[41] indicate that penicillin and sulfonamides, although given early and in adequate amounts, were without effect in many cases of septic abortion. Many authoritative data indicate that there are enzymelike penicillin inhibitors.[40, 42] Many of the pathogenic organisms do not produce enzymelike penicillin inhibitors, but are found in combination with secondarily invading organisms which do produce the inhibiting factor, thus neutralizing the bacteriostatic activity of the penicillin against the primary invading penicillin-susceptible organisms.[40, 43]

The production of the penicillin inhibitors is probably not the only factor determining bacterial resistance to penicillin. Accumulations of pus, dead tissue, and fibrin definitely offer mechanical interference to the diffusion and efficiency of penicillin.[44]

Obviously, removal of the necrotic intrauterine debris is necessary to eliminate the source of sulfonamide inhibitor substances, and to remove the chemical and mechanical barriers to penicillin. In addition, removal of the necrotic material eliminates the favorable environment for the less invasive bacteria. The virulent (Group A) hemolytic streptococci tend, in their early stages, to spread rapidly through the tissues without causing necrosis in the infected area. Fortunately, in this small group, the sulfonamide drugs and antibiotics produce their most striking effects.[39, 45, 46]

It was with this information and reasoning that the following procedure was developed.

Procedure

On admission to the hospital each case of incomplete abortion was subjected to the following:

1. Examination:
   a. Temperature, pulse, respiration rates, blood pressure determination, and interne's physical examination.
   b. Laboratory examination of peripheral blood.
   c. Sterile, bimanual, pelvic examination to aid in determining whether or not the infection had extended beyond the uterus.
2. Removal of loose tissue present in the vagina or cervix with sponge forceps.
3. Culture taken from within the uterine cavity.

If, from laboratory studies and clinical impression, it was deemed necessary, a citrated blood transfusion of 350 c.c. to 500 c.c. was given and repeated when required.

Culture swabs containing material from within the cervix were streaked on blood agar plates and broth culture media were inoculated. Both were incubated and the blood agar plates observed in twelve and sixteen hours for characteristic minute colonies surrounded by a wide zone of hemolysis. The Lancefield microprecipitin method was used to determine whether or not Group A streptococci

were present in the uterine cavity. All of this information was usually available within eighteen to twenty-four hours after the culture was taken. In 95 cases thus examined, three were found harboring Group A hemolytic streptococci.

During the twenty-four to thirty-six hour period of observation, an injection of one c.c. of obstetric Pituitrin intramuscularly and Ergotrate, mg. 0.2 by mouth, every four hours were administered. If the patient's oral temperature was greatly elevated (100.2° F. or more) after admission, one of the sulfonamide group of drugs in adequate doses was given orally. Later in the series, penicillin was used either alone, or in combination with sulfadiazine. Absence of adnexal involvement or pelvic abscess formation was believed to be due to the liberal use of chemotherapy and particularly after penicillin was added to the treatment regime.

At the end of twenty-four to thirty-six hours, the cervical culture and the Lancefield precipitin reaction results were reported. In the absence of Group A hemolytic streptococci in the uterine cavity and with the abortion again judged to be incomplete as evidenced by continued vaginal bleeding and lower abdominal cramping, the patient was then prepared for a curettement under anesthesia.

Prior to actual curettage, the depth of the uterine cavity was carefully measured and then the cavity systematically curetted with a large curette. It was felt that perforation would be less likely to occur when a large curette was employed.

A series of 95 cases of incomplete abortion was treated by the so-called radical method. Patients in this group were not dismissed from the hospital until the oral temperature was normal for 24 hours and other signs of toxemia were absent for the same period. The sooner the cases were treated in this manner, the shorter the period of morbidity. In this group of cases the average number of postoperative hospital days was 4.0; the number of days of morbidity averaged 3.1, while there were no deaths.

The following table is included in an attempt to compare the method reported herein with cases cared for by more conservative measures, where bacteriologic procedures were not employed to aid in the selection of cases. (Table I.)

TABLE I. TREATMENT RESULTS COMPARED

	SURGICAL	SURGICAL[1] (J. D. H.)	CONSERVATIVE[2] (J. S. H.)	CONSERVATIVE[1] (J. D. H.)
Number of cases	95	55	100	34
Average days in hospital	4.9	5.1	11.3	12.3
Days of morbidity	3.1	3.8	7.8	9.1
Cases subsequently curetted	3	0	24	18
Cases with group A organisms	3	Not determined	Not determined	Not determined
Mortality	0	*1.8% (1)	3% (3)	**2.1% (1)

[1]Jefferson Davis Hospital.
[2]John Sealy Hospital
*infection.
**hemorrhage.

The three patients whose cervical cultures contained Group A beta hemolytic streptococci were treated by small repeated transfusions, oxytocics, and adequate sulfonamide and/or penicillin until the intrauterine cultures failed to reveal the presence of Group A organisms and the clinical picture was not

that of extreme sepsis. If the abortion was judged to be incomplete at this time, a curette débridement was performed. Subsequently, all three cases were curetted.

These results indicate that, with a careful selection of cases by now-available and not too technical methods, a larger number of patients can be treated surgically for incomplete abortion, thereby appreciably reducing the mortality and morbidity rates and period of hospitalization. Furthermore, the sooner the curettement is performed after the abortion, the shorter the period of postoperative morbidity and hospitalization.

References

1. Maternal Mortality Reports in the United States, 1941, Children's Bureau, 1943.
2. Maternal Mortality Rates for 1943 and 1944, Child **11**: 151, 1947.
3. Gordon, O. A., Jr.: J. A. M. A. **82**: 1021, 1924.
4. Cron, R. S., and Lehmann, A. H.: Wisconsin M. J. **34**: 327, 1935.
5. Watkins, R. E.: West. J. Surg. **44**: 338, 1936.
6. McCord, J. R.: New Eng. J. Med. **217**: 776, 1937.
7. Peckham, C. H.: Surg., Gynec. & Obst. **63**: 109, 1936.
8. Stewart, R. E.: Am. J. Obst. & Gynec. **29**: 872, 1935.
9. Studdiford, W. E.: New York State J. Med. **39**: 1274, 1939.
10. Galloway, C. E., and Paul, T. D.: Am. J. Obst. & Gynec. **37**: 246, 1939.
11. Dunn, R. D.: Am. J. Obst. & Gynec. **33**: 149, 1937.
12. Crossen and Crossen (Text): Diseases of Women, ed. 9, St. Louis, 1941, The C. V. Mosby Co.
13. Ravenscroft, J. W.: California and West. Med. **57**: 346, 1937.
14. Posmore, H. S.: J. Obst. & Gynaec. Brit. Emp. **44**: 455, 1937.
15. Polak, J. O.: Gynec. and Obst. Monograph Series, New York, 1928, D. Appleton Co.
16. Cooke, W. R.: Essentials of Gynecology, Philadelphia, 1943, J. B. Lippincott Co.
17. Sandusky, W. R., Pulaski, E. J., Johnson, B. A., and Meleney, F. L.: Surg., Gynec. & Obst. **75**: 145, 1942.
18. Schwarz, O. H., and Dieckmann, W. J.: Am. J. Obst. & Gynec. **13**: 467, 1927.
19. Soule, S. D., and Brown, T. K.: Am. J. Obst. & Gynec. **23**: 532, 1932.
20. Carter, B., and Jones, C. P.: South. M. J. **30**: 298, 1937.
21. Altemeier, W. A.: Am. J. Obst. & Gynec. **39**: 1038, 1940.
22. Brown, T. K., and Hunt, G. A.: Am. J. Obst. & Gynec. **32**: 804, 1936.
23. Colebrook, L. T.: J. Obst. & Gynaec. Brit. Emp. **43**: 691, 1936.
24. Studdiford, W. E.: Bull. New York Acad. Med. **17**: 567, 1941.
25. Topley, W. C., and Wilson, G. S.: Principles of Bacteriology and Immunity, ed. 2, Baltimore, 1937, William Wood & Company.
26. Johnson, C. G., and Talbot, T. D.: Am. J. Obst. & Gynec. **45**: 847, 1943.
27. Lancefield, R. C.: J. Exper. Med. **57**: 571, 1933.
28. Swift, H. F., Lancefield, R. C., and Goodner, K.: Am. J. M. Sc. **190**: 445, 1935.
29. Lancefield, R. C., and Hare, R. J.: J. Exper. Med. **61**: 335, 1935.
30. Zinsser, H., and Bayne-Jones, S.: Text Book of Bacteriology, ed. 8, New York, 1939, D. Appleton-Century Co.
31. Adair, F. L.: Editor (Monograph) Maternal Care Complications, Univ. Chicago Press, Chicago, 1938.
32. Douglas, R. G.: Am. J. Surg. **35**: 352, 1937.
33. Dunn, H. L.: Dept. of Commerce, Bureau of Census, Special Reports **15**: 431, 1942.
34. Lockwood, J. S.: Surg., Gynec. & Obst. **72**: 307, 1941.
35. Woods, R. D.: Brit. J. Exper. Path. **21**: 74, 1940.
36. Laudy, M., and Dicken, D. M.: J. Biochem. **146**: 109, 1942.
37. Laudy, M., Larkum, A., Oswald, E. J., and Streightoff, F.: Science **97**: 265, 1943.
38. Weil, G. C., Whitaker, D. W., and Ruebridge, H. M.: Am. J. Surg. **5**: 374, 1942.
39. Olson, H. J., Laymann, A. H., Mietus, A. C., and Mitchell, R. M.: Am. J. Obst. & Gynec. **45**: 672, 1943.
40. Bondi, A., Jr., and Dietz, C. C.: Proc. Soc. Exper. Biol. & Med. **56**: 132, 1944.
41. Jones, W. N.: South. M. J. **39**: 646, 1946.
42. Bondi, A., Jr., and Dietz, C. C.: Proc. Soc. Exper. Biol. & Med. **56**: 135, 1944.
43. Rammelipamp, C. H., and Keefer, C. S.: J. Clin. Investigation **22**: 425, 1943.
44. Lankford, Charles: Personal Communication.
45. Kirby, Wm. M.: Science **99**: 452, 1944.
46. Frasier, C. N.: Texas Reports on Biol. and Med. **2**: 385, 1944.

Discussion

DR. RUDOLPH W. HOLMES, Charlottesville, Va.—It happened to have been my fortune to have been appointed chairman of The Committee on Criminal Abortion of the Chicago Medical Society. As a result of this, I became an honorary coroner's physician and deputy coroner for some five or six years. I witnessed the autopsies on the majority of the women who actually or putatively died from the criminal assault. I firmly believe that there are as many, if not more, criminal operations performed as there are near-term babies. A woman who glibly acknowledges the fact may be believed; if she denies the origin too many times she is lacking in veracity.

As my recollection goes, at least one-quarter of the women who came to the postmortem table showed marked traumatisms of the genital tract—mostly uterine perforations, though cervical and vaginal injuries were frequent. The lamentable picture is that at least one-half of these injuries were produced by overzealous, perhaps unskilled addicts in the use of the sharp curette or placental forceps. The pity of it is, that, no matter how conclusively it is revealed that the abortionist had operated, the defense lawyer will invalidate all testimony by averring the second doctor was responsible for the trauma. Recamier introduced the curette in 1802. I have asserted for years that it is a physically impossible feat completely to scrape the uterine mucosa in or out of the pregnant state: true, gross fragments of the decidua may be caught and removed, but that is all. Where are the gynecologic pathologists and clinicians that they have not heard of the *reaction zone of Braum!* This reaction is merely the inflammatory reaction which occurs in all localized infections, whether there be an abscess forming or actually in existence. What surgeon would open an abscess and then curette the wall! An infected uterus is only a self-draining abscess.

DR. P. B. RUSSELL, Memphis, Tenn.—I corroborate Dr. Holmes' remarks about the rupture of the uterus. I have seen two very good operators go completely through the fundus or some other part of the uterus while curetting.

I wish to congratulate Dr. Morse upon his report and about his remarks concerning the examination and making cultures, in particular. To me this is one of the most important things in the consideration of a criminal abortion. Most of these patients are infected when they come in and it is almost unbelievable that anyone would invade the uterine cavity without first taking a smear and/or culture from the cervical canal, and thereby try to determine the lethal organisms. Last November I read a paper, during the Southern Medical Association Meeting, in which I reported 3,379 cases of abortion. In this series there were 202 operative procedures, and 91 of these were proved not to be cases of pregnancy, based upon the report of the pathology department. Eight of the patients in this series were curetted more than once. Some may argue, if you do not curette these patients, there is the possibility of a chorionepithelioma developing at a later date. Out of a very large series investigated, there was one in the 113,238 cases with this condition and she was not a case of an abortion, but one of premature delivery. Therefore, I refute the argument it is better to curette than to risk the development of a chorionepithelioma if surgery is omitted. Too, in a patient with an endometritis and fever, one does not curettte the patient, and yet, many will curette a patient with an infected abortion. I do not think it is wise to do so, routinely.

DR. ROBERT J. CROSSEN, St. Louis, Missouri.—As early as 1927 we have treated infected abortion by gentle removal of any retained secundines by means of a sponge forceps. This is followed by intrauterine douche of 1:2000 potassium permanganate. By culturing each case, the anaerobic bacilli were usually found to be the source of the infection. These patients were able to leave the hospital in five to seven days. Some years ago at Washington University we started using instillation of mercurochrome in glycerine in the vagina of all cases in labor and found that it reduced the morbidity. Recently we have been using 1 per cent neutral acriflavine in glycerine.

DR. CHARLES GALLOWAY, Evanston, Ill.—I published a paper not long ago based on 1,114 cases of abortion admitted to the Evanston Hospital. This included 643 incomplete abortions and 605 of those were curetted. We had one death due to hemorrhage but this patient was practically exsanguinated by the time she reached the hospital.

The best way to treat such a patient is to empty the uterus early, get the cervix closed down and the case terminated so that she may again resume her normal life. One of the best ways to infect your patient is to allow the uterus to remain open and all the vaginal bacteria to enter this very fertile field.

DR. MORSE (Closing).—The three cases that showed group A hemolytic streptococci were admitted criminal abortions.

All agree that the uterus should be curetted if there is profuse bleeding. About 15 per cent of all incomplete abortions are curetted because of hemorrhage in the presence of fever. Why is there such a change in attitude when hemorrhage is not a prominent factor?

We are familiar with the late sequelae of incomplete abortion: the menstrual rhythm is often disturbed, and many of these women subsequently become sterile. Many of the late and remote complications can be prevented if the uterus is completely emptied early.

I hope that this paper has stimulated a renewed interest in the whole problem of abortion. The statistics indicate that something must be done. The 1945 statistics reveal that the abortion mortality has changed little when compared to the 1944 rate.

AMEBIC VAGINITIS*

B. Bernard Weinstein, M.D., and John C. Weed, M.D., New Orleans, La.

(From the Department of Gynecology, Tulane University, School of Medicine, and Touro Infirmary, and the Department of Gynecology and Obstetrics, Ochsner Clinic)

AMEBIC vaginitis is a rare vaginal infection first reported in the United States in 1944 by de Rivas.[1] In 1943, Bickers,[2] in a study of 200 cases of leucorrhea, observed that 0.5 per cent were caused by *Endameba histolytica* but did not report any cases. Bacigalupo and associates[3] of Argentina reviewed the literature in 1942 and described one case. Since then cases have been reported by May,[4] Morse and Seaton,[5] Cleland[6] and de Rivas.[1] It is interesting to note that in 1928 Hegner[7] reported the presence of *Endameba nana* in vaginal washings obtained by Hartman in the course of some experiments on rhesus monkeys.

It is well known that the incidence of amebic infestation in the United States is high.[8] The incidence of amebiasis in routine stool examinations on all patients admitted to Touro Infirmary ranges from 3 per cent to 5 per cent. Despite the numerous cases of amebiasis encountered among the admissions to Touro, there has been no instance of amebic vaginitis diagnosed prior to the four cases to be reported in this paper.

Although only ten cases of amebic vaginitis were found in a review of the literature from 1916 through 1946, within a period of nine months in 1946 we have treated four patients with this condition. The first patient was seen in April, 1946; this case was reported by one of us (B. B. W.) at a meeting of the Obstetric and Gynecologic Residents of Touro Infirmary. The second patient was admitted in June, the third in August, and the fourth in December, 1946. Although thorough examinations for parasites have been made since, no further instance of amebic vaginitis has been encountered.

Report of Cases

Case 1.—Mrs. C. E., aged 29 years, was seen in April, 1946, complaining of irregular bloody vaginal discharge first noticed in December, 1945. It was unaccompanied by pain or pruritus and did not have a particularly foul odor. It occurred more or less continuously throughout the month with no relation to the menstrual period. The patient consulted her local physician in January, 1946, because of dyspareunia and was given several types of soothing douche powders which she used for the next two months with no appreciable improvement. There was no history of intestinal disorders.

Pelvic examination revealed a serosanguineous discharge. The cervix had an irregular erosion, eccentrically placed, occupying an area of 2 cm. by 3 cm. between five and nine o'clock on the cervix. The uterus was slightly enlarged, exquisitely tender and freely movable.

*Read before the meeting of the Central Association of Obstetricians and Gynecologists, Louisville, Ky., Oct. 25, 1947.

The vagina appeared to be slightly eroded in several places. Examination of the vaginal discharge, both by dry and hanging drop smears, disclosed the active form of *E. histolytica.* The presence of amebas was discovered in the stool. Treatment consisted of a course of Diodoquin and emetine and vaginal insufflation of Vioform powder once daily for two weeks. The local lesion cleared up rapidly with the use of Vioform powder and cleansing douches.

CASE 2.—Mrs. L. P., aged 35 years, was admitted to Touro Infirmary in June, 1946, because of irregular vaginal bleeding which began about October, 1945, but was evidently not severe enough to cause the patient to seek medical advice until March, 1946. At this time the discharge became progressively worse and there was definite increase in vaginal tenderness until the patient could hardly tolerate speculum examination of the vagina. The discharge was a bloody, mucous, granular type which did not cause pruritus. The patient had passed blood in the stool on one occasion.

Pelvic examination revealed a bloody vaginal discharge. There was a peculiar type of erosion well away from the external os of the cervix on the right side; this was cauterized at the time of the first examination. The uterus was enlarged, pulled to the right side and thought to contain a fibroid.

Two weeks later the patient still had a bloody vaginal discharge. The cervical lesion showed no improvement and was at this time painted with a 50 per cent solution of silver nitrate. Various types of local treatment were instituted for the next two months during which time an organism consistent with *Hemophilus of Ducrey* was isolated from the vaginal discharge. The patient was then given a twenty-one-day course of sulfadiazine therapy with no results.

On June 13, 1946, the patient was admitted to the hospital for streptomycin therapy. Four days after admission a stool specimen was reported positive for *E. histolytica.* The vaginal discharge contained numerous trophozoites of *E. histolytica.* The streptomycin was discontinued and the patient was discharged from the hospital and given a 5 per cent solution of chiniofon to instill into the vagina twice daily. She was also given a course of Diodoquin and emetine. Within five days the local irritation and bloody discharge had improved remarkably. The patient, seen a month later, was completely cured. She had no vaginal tenderness, no discharge, and no areas of ulceration.

CASE 3.—Miss R. E. C., aged 21 years, presented herself in August, 1946, with the chief complaints of pruritus and "menstruating for three months."

The patient gave no history of any intestinal disorder. She had begun to menstruate at the age of 15 and menses were regular, occurring every 29 days. Even during the past three months, despite the fact that "she menstruated every day" she also had regular bleeding periods at the time the normal menses were to be expected. On examination, a bloody vaginal discharge was observed. The vagina appeared to have one or two small granular areas from which there was slight oozing. The cervix had an eccentrically placed erosion about 0.5 cm. in diameter, centering around nine o'clock and a smaller lesion at four o'clock. A smear was made of the discharge and the trophozoite form of *E. histolytica* was found. The patient received treatment similar to the previous cases and the infection subsided within three weeks; she has had no recurrences. Repeated stool examinations over a period of several months failed to demonstrate the cysts or trophozoites of *E. histolytica.* In January, 1947, the patient had a sudden attack of severe bloody diarrhea and the trophozoite form of *E. histolytica* was demonstrated in the stools. She was treated for intestinal amebiasis, and, at that time, careful examination of the vagina and cervix revealed no recurrence of vaginal and cervical infections.

CASE 4.—Mrs. E. C. P., aged 46 years, entered Touro Infirmary in December, 1946, because of a bloody vaginal discharge. At the age of 42, radium castration for fibroids was done elsewhere. She did not have pruritus, and there was no odor to the discharge. What concerned her was that she "was starting to menstruate again" after she had been assured that the radium given her would make this impossible.

Examination revealed a cystocele, a rectocele and a copious amount of bloody vaginal discharge. The vagina, when cleansed, showed pronounced senile vaginitis and was rather friable. On the cervix there was a continuous rim of erosion from about two o'clock to nine o'clock, placed at the outer periphery and about 1 cm. wide. This was granular and bled easily. The uterus was about two and a half times the normal size and contained multiple fibroids. No adnexal masses were found. Cervical biopsy revealed no evidence of carcinoma. A Papanicolaou smear also disclosed no evidence of malignant cells. Approximately a week later the patient again had a large amount of bloody vaginal discharge. Routine vaginal smears had not been previously obtained because the bleeding was attributed to the cervical lesion and the senile vaginitis and cervical carcinoma rather than vaginitis was suspected. Careful smears were then made and the trophozoite form of *E. histolytica* was demonstrated. Although the patient had given no history of intestinal irregularities, when questioned more carefully at this time, she admitted that she had had an attack of alternating diarrhea and constipation approximately a year and a half before and that she had spent about six months at that time in Central America. She had received no treatment for this intestinal disorder and she stated that after her return to the United Sates it had cleared up. Stool examination revealed the presence of *E. histolytica.* Treatment consisted of Vioform powder insufflation into the vagina, cleansing douches, and the systemic administration of Diodoquin and emetine. The vaginal discharge disappeared in approximately ten days. The cervix was clear when the patient was examined about a month later.

When the results of both the stool and vaginal examinations were repeatedly negative for *E. histolytica,* the patient was given some estrogenic suppositories to relieve the senile vaginitis and reported about four weeks later that she was having no symptoms. In June, 1947, after a careful examination revealed no ameba in the stool and vagina, a hysterectomy and plastic repair were performed with an uneventful convalescence.

Discussion

The following significant observations have been made almost constantly on these patients. Their complaint is usually of a serosanguineous or frankly bloody vaginal discharge, not associated with pruritus. There is a peculiar ulcerated lesion of the vagina and frequently of the cervix. The cervix is involved in approximately 70 per cent of the reported cases. In those cases which have been reported the cervical lesion is usually eccentrically placed and away from the external cervical os. There is a relatively shallow, granular, not uncommonly purulent area, which is usually extremely friable. The uterus is often enlarged, soft, engorged, and tender. In one of the cases in the literature,[9] the diagnosis was made at autopsy and there was considerable involvement of the uterus. It is possible that many or all the cases in which the uterus is enlarged, soft, and tender have similar uterine involvement. Uterine aspiration was not done in any of the reported cases. The cervix is usually enlarged, engorged, soft, and extremely tender on palpation. These lesions are friable and bleed readily and persistently. It would be easy to confuse them with any of the granulomatous lesions, particularly carcinoma or infection from *Hemophilus of Ducrey.* In most of the reported cases,[3-6] biopsy or scrapings were obtained at some time in an attempt to determine the causative factor. The trophozoite form of *E. histolytica* can be readily identified in a wet vaginal smear[8] and most of the reported cases, as well as all of ours, have been associated with amebic infestation of the intestines.

Treatment is still relatively empiric since so few cases have been reported; a variety of methods of treatment has been used. The local lesion will probably clear up spontaneously if the patient is given systemic therapy for amebic infection. However, the cases reported in this paper have responded to insufflation of the vagina with amebacidal agents, amebacidal douches, or both, combined with systemic therapy for the intestinal amebiasis.

Summary

1. Four cases of amebic vaginitis and cervicitis are reported.

2. These cases are characterized by bloody vaginal discharge without pruritus and the presence of a granular lesion in the vagina or eccentrically placed on the cervix.

3. The trophozoite form of *E. histolytica* can be demonstrated in the vaginal secretion and usually also in the stool.

4. These cases respond well to the usual amebacidal agents.

5. It is possible that cases of amebic vaginitis are overlooked or confused with other vaginal lesions.

References

1. de Rivas, D.: Am. J. Trop. Med. **24**: 185-187, 1944.
2. Bickers, W.: Virginia M. Monthly **70**: 135-140, 1943.
3. Bacigalupo, J., Julien, E. M., and Puga, C. R.: Semana méd. **2**: 525-533, 1942.
4. May, M. Y.: Indian M. Gaz. **78**: 250, 1943.
5. Morse, E. M., and Seaton, S. P.: Am. J. Trop. Med. **23**: 325-326, 1943.
6. Cleland, J. B.: J. Trop. Med. **47**: 54-55, 1944.
7. Hegner, R.: J. Parasitol. **16**: 91-92, 1929.
8. Craig, C. F., and Faust, E. C.: Clinical Parasitology, ed. 4, Philadelphia, 1945, Lea & Febiger.
9. Nisioka, T.: J. Chosen M. A. (Abstr. Sect.) **30**: 17-19, 1940.

Discussion

DR. LAMAN GRAY, Louisville, Ky.—It is exceedingly interesting to have one of the first reports of amebic vaginitis before this Society. We have known amebiasis largely as a disease of the gastro-intestinal tract and liver, estimated by some to involve 1 to 10 per cent of the population at large. Also, there have been reports of lesions of the skin, simulating luetic ulcers. Some forms of arthritis have been attributed to amebiasis. It is most logical that the infection should occur in the vagina, because of its close proximity to the rectum.

Amebiasis of the rectum is said to be characterized by deeply punched-out ulcers with overhanging edges, the base being covered with thick, yellow exudate. The mucous membrane is said to bleed quite easily from trauma. These surface findings do not represent the true pathology, which is infiltrative inflammation, chiefly in the submucosa. We would expect similar pathology in the vagina.

Since relatively few laboratory workers are competent to identify *Endomeba histolytica*, it behooves each of us to study carefully the characteristics of this organism in order that we may identify it in our routine fresh preparations of the vagina.

Original Communications

TREATMENT OF TRICHOMONAS VAGINALIS WITH TYROTHRICIN*

C. Gordon Johnson, M.D., F.A.C.S., New Orleans, La., J. William Douglas, M.D., Pensacola, Fla., and Ruth Y. Mayne, M.S., New Orleans, La.

(From the Departments of Obstetrics and Gynecology, Tulane University of Louisiana, School of Medicine, and the Charity Hospital of Louisiana)

SINCE its first description clinically, the treatment of trichomonas vaginitis has been controversial. There have been a multiplicity of methods reported in the literature, this alone being *prima facie* evidence that none so far described have proved to be outstanding.

The patients for this study were observed in the Obstetrical Clinics of the Charity Hospital of Louisiana at New Orleans. Routine vaginal smears for *Trichomonas vaginalis* were made in 1,197 patients. The results of this study are shown in Table I.

It was interesting to note that of sixty patients having trichomonas vaginalis who were carefully questioned regarding symptoms, 45, or 75 per cent, gave a positive answer. These symptoms varied from a moderate discharge with little pruritus to a heavy one with marked itching and burning.

Treatment was carried out exclusively by the patient herself. She was instructed not to take douches during the intervals of treatment. She also was advised not to have intercourse; this, however, was difficult to control and was most probably not followed very well. There were two main objectives in this study. The first was to determine the value of tyrothricin in treating trichomonas vaginitis. The second objective was to determine the value of treatment by self-medication alone.

Tyrothricin is an alcohol-soluble, water-insoluble, extract of *Bacillus brevis*. It was first isolated and described by Dubos. It was used in this study in the form of suppositories having the following composition:

V-86 contains a water-soluble base, from which the suppositories were made, plus 5 mg. of tyrothricin per suppository. Its pH is 5.3.

V-82 and V-24 are similar to V-86 in that they are a combination of the water-soluble base but in addition contain proper amounts of lactic, citric, and boric acids. They contain no tyrothricin. The pH of V-82 is 1.5 and that of V-24 is 2.8.

V-32 and V-23A contain the water-soluble base with lactic and boric acids and, in addition, 5 mg. of tyrothricin. V-32 has a pH of 2.05 and V-23A a pH of 2.65.

Table I. Incidence of Trichomonas Vaginalis

	White	Colored	Total
Total examined	255	942	1197
Positive	40	281	321
Per cent positive	15.7	29.8	26.8

*The Tyrothricin used in this study and funds for the survey were supplied by Sharp & Dohme, Inc., Philadelphia, Pa.

In order to determine the change in the vaginal pH that would take place in the presence of the acid suppository, five patients having no vaginal infection were tested with this suppository. The pH of this suppository was 1.5. The results of this test are shown in Table II.

TABLE II

VAGINAL pH BEFORE TREATMENT	5 HOURS LATER	11 HOURS LATER	24 HOURS LATER
7	3	4.5	6
7	5	5	6
5	2	3-4	5-6
6	4	4	5
7	4	4	5-6

By this test it was apparent that the acid suppository did considerably lower the vaginal pH for about twelve hours. At the end of twelve hours the pH had returned almost to the same as before the insertion of the suppository. This degree of change, however, should be sufficient to produce any results that might take place from increased acidity.

A total of fifty-six patients were treated with one of the three suppositories. There were eleven white and forty-five colored patients. The results of treatment are shown in Table III and seem to indicate similar findings with both acid tyrothricin and acid control. As a matter of fact, better results were obtained from the acid control suppository. The number of cases treated with bland tyrothricin is too small to evaluate. There were thirty-seven patients given a known duration of treatment and follow-up examination. Fourteen, or thirty-seven per cent, of these were classed as improved. This meant that during the course of treatment there were relief from symptoms and negative vaginal smears. After cessation of treatment, however, the symptoms and positive smears promptly returned.

TABLE III

NUMBER TREATED	DURATION OF TREATMENT	DRUG USED	IMPROVED	CURED	FAILED	DID NOT RETURN
23	2 to 10 wk.	Acid tyrothricin V-32	3	3	5	12
8	2 to 10 wk.	Acid tyrothricin V-23A	2	5	1	0
15	2 to 10 wk.	Acid control V-24	5	4	2	4
7	2 to 10 wk.	Acid control V-82	3	1	1	2
3	2 to 10 wk.	Bland tyrothricin V-86	1	0	1	1
Total 56			14	13	10	19

Thirteen, or 35 per cent, of the thirty-seven known patients were stated to be cured. This meant that they remained symptom free and had negative smears for two weeks after treatment was discontinued. Positive smears after that time were considered reinfections but could also probably be considered recurrences. Ten, or 27 per cent, of the thirty-seven known cases were considered failures, symptomatically and from smear examination.

The number improved or cured does not compare favorably with results of other drugs. This perhaps may be explained by the fact that all treatments were carried out by the patients themselves. Better results could possibly have been obtained if the therapy had been continued longer.

A large number of patients complained of considerable vaginal burning and irritation from both acid tyrothricin and acid control suppositories. In some instances, it was necessary to discontinue the use of these suppositories because of the burning.

Summary and Conclusions

Tyrothricin in the form of an acid suppository was used in the treatment of a group of patients having trichomonas vaginitis. A similar group was treated with an acid suppository that did not contain tyrothricin.

The results indicate that the use of tyrothricin in the treatment of trichomonas vaginitis is unsuccessful. This antibiotic, in suppository form, was not as effective as most common methods now in use.

KRUKENBERG TUMOR WITH OSTEOPLASTIC METASTASES

JOSEPH H. ZEIGERMAN, M.D., M.Sc. (MED.), PHILADELPHIA, PA.

(From the Department of Obstetrics and Gynecology, Graduate School of Medicine of University of Pennsylvania)

AMONG the numerous articles written on Krukenberg tumors no cases were found where osteoplastic metastases were noted. Following is the report of a case where massive osteoplastic metastases were seen.

H. L., a married, white multipara, 27 years old, was admitted to the Graduate Hospital in August, 1944, complaining of vaginal bleeding and a mass in the abdomen. Her medical history included a salpingo-oophorectomy for tumor of the right ovary at another hospital in August, 1943. Her postoperative convalescence was uneventful and she left the hospital on the fourteenth day. She had remained in good health for one year and had not returned for follow-up care. The pathologic report was as follows:

Specimen is a solid mass which has been previously bisected. It is 11 by 7 by 5 cm. The cut surfaces are pale yellow brown. Attached is a Fallopian tube which is hemorrhagic; it measures 3.5 by 2.5 by 2.5 cm. The microscopic picture is that of a solid tumor presenting an interesting and very unusual picture. In some regions there are solid islands of what superficially appear to be epithelial cells. The supportive structure of the ovary appears to be composed of dense, elongated cells, resembling fibroblasts. In other regions, the follicular arrangements of cells are more definite in the form of cysts, with large empty spaces lined by several rows of follicular cells.

Comment: The exact nature of this tumor cannot be determined at this time. It was the impression that the tissue resembled in part, a thecal cell tumor of the ovary and in other regions, that of folliculoma. The slides were shown to other pathologists, all of whom differed to some extent in the diagnosis, and none of whom was very definite in his opinion. One pathologist actually thought that the epithelium-like cells were truly epithelial nests and the tumor represented a Krukenberg tumor of the ovary; others felt that it represented some endocrine or developmental tumor of the ovary.

On the present admission to Graduate Hospital, University of Pennsylvania, August, 1944, the patient complained of vaginal bleeding and a mass in the abdomen. The general examination was essentially negative. The pelvic examination revealed a freely movable, firm, globular mass, the size of a large grapefruit, attached to the uterus by a pedicle. The mass was thought to be a tumor of the left ovary or a pedunculated fibroid. At operation an ovarian cyst the size of a large grapefruit, half twisted on its pedicle, was removed together with the uterus.

The ovarian tumor was 18 by 11 by 8 cm., in its greatest diameter. The capsule was thick, with a number of scarlike depressions, whitish in color, containing several cysts, the largest 3 cm., in diameter. The cut surface was pink with a background of translucent edematous tissue with rounded opaque structures. Microscopy (Dr. Case). Mucoid carcinoma of the Krukenberg type (Fig. 1).

Following the operation there were no complications except for several transfusion reactions. During her stay in the hospital an attempt was made to locate the primary growth

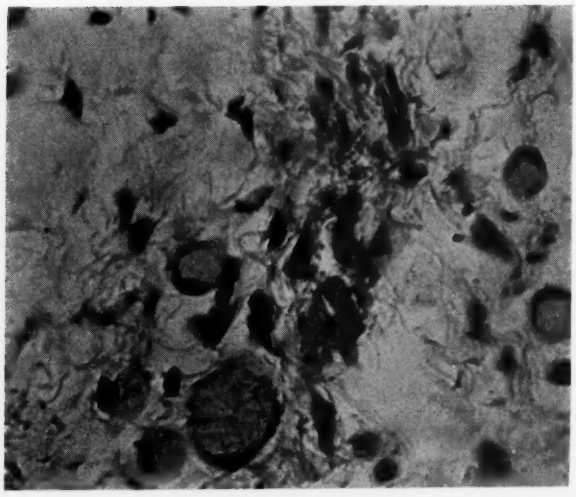


Fig. 1.—Mucoid carcinoma of the Krukenberg type with the characteristic signet-ring type of cells.

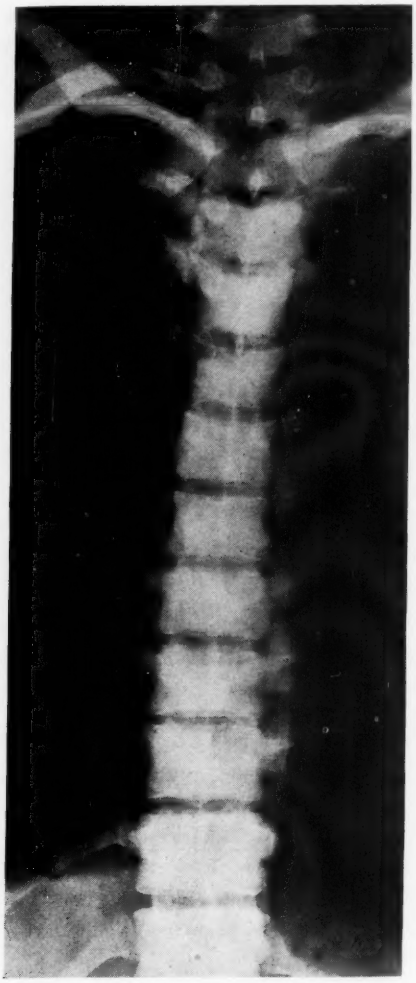


Fig. 2.—Chalky white appearance of dorsal spine is characteristic of osteoplastic metastases.

of the Krukenberg tumor in the intestines. However, all studies of the gastrointestinal tract were negative. She was discharged in fairly good condition and resumed her household duties a few weeks later. She was treated daily by x-ray through two portals, 200 R to each portal, alternating anteriorly and posteriorly. A total of 2,000 Roentgen units (as measured in air to each portal using 190 K.V., 10 M.A., 50 cm., distance, 0.5 cm., copper, and 1 mm., aluminum filtration) was given. The lower abdominal portals measured 15 by 20 cm., the upper 10 by 15 cm. Three courses were proposed but only one course was completed before the death of the patient.

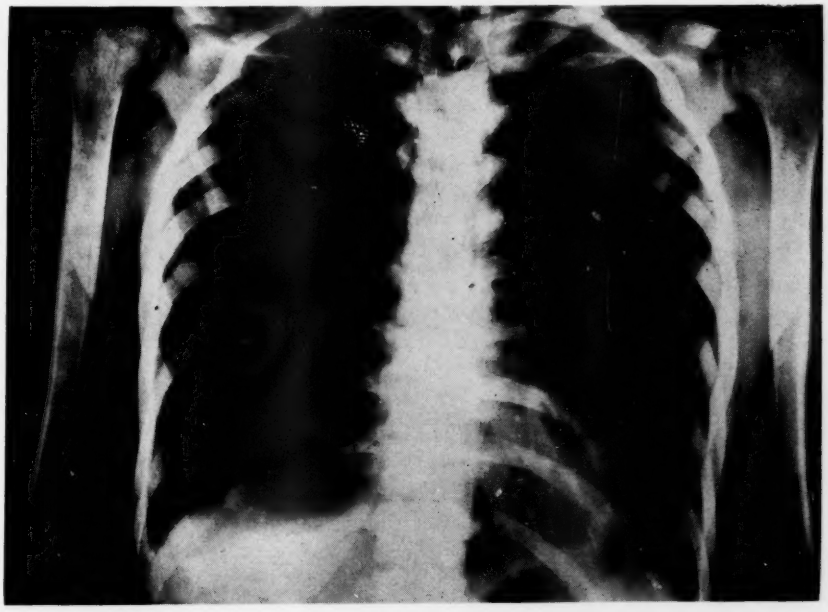


Fig. 3.—Spotty mottling involving the entire dorsal spine, upper ends of the humerus and ribs, due to osteoplastic metastases.

She enjoyed good health the following five months, gained weight, and was not offering any complaints. At the end of the fifth month she began to complain of pain in the dorsolumbar spine and both thighs (Fig. 2).

An x-ray survey of the entire skeleton at this time showed varying degrees of osteoplasia, involving all the ribs, the clavicles, the scapulae, the upper three-fourths of both humeri, and most of the cervical vertebrae (especially the second and seventh). There was also a very slight increase in density of the pelvic bones, especially the right and left ischium. The skull and the bones distal to the elbows and knees were not involved (Fig. 3).

From here on her health began to fail rapidly. There was a progressive anorexia with loss of weight, emaciation, secondary anemia and excruciating pains in the involved bones. Patient died three months after the onset of the metastatic bone symptoms, and eight months after the second operation. Autopsy was not obtained.

Comment

In the few reported cases of ovarian carcinoma when bone metastases were seen, the bone pathology was predominantly a process of osteoclasia. In our case, however, we found an opposite picture of bone pathology, namely, osteoplasia. The cause of this unusual deviation is not known. One may consider the relationship of hormones, since it is known that estrogen may cause a deposition of calcium in the secondary trabeculae of the bone.

References

1. Geshickter, C. F.: Am. J. Cancer, 1936, a-p 511, b-p. 489, c-p 525, d-p 539, e-p 544.
2. Levin, I.: Ann. Surg. **65**: 326, 1917.
3. Moore, A. B.: Am. J. Roentgenol. N. S. **6**: 589-593, 1919.
4. Recklinghausen, V. F.: F. Diefibrose oder deformierende Ostitis, die Osteomalacie und die osteoplastische Carcinose in Ihren gegenseitigen Beziehungen, Festschrift zu Rudolph Virchow's 71 Geburtstage 1891, p. 71.

1836 Delancey Place

MASSIVE GASTRIC HEMORRHAGE IN PREGNANCY

JOHN CARANGELO, M.D., HARTFORD, CONN., AND THOMAS D. EFSTATION, M.D.
BIRMINGHAM, ALA.

(From the Department of Obstetrics and the Department of Pathology of the Medical College of Alabama and the Jefferson-Hillman Hospital)

FOUR cases demonstrating the unusual complication of massive hemorrhage during pregnancy at term are herein reported. Review of the literature reveals that this is not a common complication. Greely and Stubenbord,[1] in 1941, reported one case of a 31-year-old patient, gravida ii, para i, at term, who had severe gastric hemorrhage, passage of tarry stools, and shock. She delivered a stillborn male fetus, following which she had an uneventful recovery.

Preiss,[2] in 1907, reported a case in which hematemesis occurred in the second and third pregnancies. These two pregnancies were complicated by the occurrence of sudden severe gastrointestinal hemorrhage as evidenced by vomiting of blood, bloody stools, and shock. In both pregnancies, the hematemesis occurred two weeks before the expected date of confinement. Both pregnancies resulted in the birth of normal stillborn male infants. The onset of labor and delivery occurred spontaneously within twenty-four hours after the bleeding.

Sturrock,[3] in 1913, reported one case of gastric hemorrhage occurring at the time of delivery.

Greenhill[4] mentions the fact that large hemorrhages may occur in the lumen of the gastrointestinal tract during toxemias of pregnancy.

CASE 1.—M. B., a Negro girl, aged 14 years, gravida i, para 0, at term, was admitted on Aug. 26, 1944, with a history of having had seven generalized convulsions.

The patient was a well developed, well nourished Negro girl in a semicomatose condition. Temperature 102.8° F., pulse 100, blood pressure 180/120. Ophthalmoscopic examination revealed no retinal changes. The heart and lungs were normal. The abdomen was compatible with a term pregnancy. Extremities revealed a 1 plus edema.

The patient was placed on modified Stroganoff regime. For the next three days the blood pressure remained around 160/120. The urinary output was considerably less than the fluid intake. Repeated urinalyses showed 3 to 4 plus albumin. Nonprotein nitrogen on admission was 27, and the uric acid was 3.48. Three days after admission the patient was rational and cooperative. On August 29, the patient's temperature rose to 103° F., respirations 40, pulse 140, heart rate 160, with a definite pulse deficit present. The patient was rapidly digitalized. Electrocardiogram at this time revealed a sinus tachycardia. She was given nasal oxygen and sodium sulfathiazole intravenously.

On August 30, the fetal heart tones were not audible. At 11 A.M., the patient had an episode of projectile vomiting of approximately 1,500 c.c. of coffee-ground fluid which was positive for occult blood. Blood pressure at this time was 130/100, pulse 140, temperature 101.6° F., respirations 40. One hour later the blood pressure was 90/60. The patient was given 1,000 c.c. of whole blood intravenously. She continued to have projectile vomiting of brownish-black fluid which remained positive for occult blood.

On August 31, she went into spontaneous labor and was delivered by low forceps of a macerated, stillborn fetus weighing 8 pounds 5 ounces. Blood loss was minimal. Total duration of labor was 4 hours and 18 minutes. Intravenous fluids and whole blood were constantly

administered. The patient continued to vomit bloody material. Blood nonprotein nitrogen and uric acid showed a gradual rise. On August 31, the nonprotein nitrogen was 97, uric acid 8. On September 1, the nonprotein nitrogen was 146. Despite continuous intravenous fluids, oxygen, and adrenal cortical extract, the patient remained in a critical condition and expired on September 2, eight days after admission to the hospital.

Postmortem Findings.—There were superficial destruction and ulceration of the mucosa of the stomach and the lower segment of the esophagus. Microscopically, there was marked congestion of the vessels with extensive hemorrhage of the wall. Some of the vessels contained thrombi, and these showed extensive necrosis. Very little inflammatory reaction was observed. The liver showed none of the lesions considered pathognomonic of eclampsia. The heart demonstrated large hemorrhages beneath the endocardium, very pronounced along the wall of the septa, which probably accounted for clinical findings in the heart. The uterus showed severe chronic endometritis in which necrosis and masses of bacteria were noted. The kidneys and spleen demonstrated acute pyelonephritis, and acute splenic tumor was present.

CASE 2.—C. B. was a Negro woman, aged 28 years, gravida i, para 0, serology negative. Her last menstrual period was Aug. 15, 1942, and expected date of confinement was May 22, 1943.

The patient was admitted to the hospital on May 28, 1943, in mild active labor. On admission, the temperature was 99° F., pulse 80, respirations 20, blood pressure 110/70. Abdomen showed the fundus to be 26 cm. above the symphysis; position right occipitoposterior; fetal heart tones in the right lower quadrant, 140 per minute. Rectal examination revealed the cervix 3 cm. dilated, presenting part at station minus two.

The patient made very slow progress during labor. She was given adequate sedation and intravenous fluids to maintain nutrition and hydration.

Two days after admission, the patient's temperature rose to 102° F., pulse 110, respirations 30. X-ray of the chest at this time was negative. Urinalysis was also negative at this time. Rise in temperature was attributed to an intrauterine infection, and the patient was placed on sulfathiazole therapy. Sedation and fluids were maintained, and, in addition, the patient was given 500 c.c. of whole blood intravenously.

On the morning of June 1, she vomited 40 to 50 c.c. of coffee-ground material which was positive for occult blood. Labor continued to progress slowly. Fetal heart tones at this time were inaudible. At 11:30 A.M. on June 1 the patient delivered a stillborn fetus weighing 8 pounds by mid forceps from the right occipitoposterior position. Blood loss was approximately 300 c.c.

Forty-eight hours after delivery, the patient vomited a considerable amount of brownish-black material which was positive for occult blood. At the same time she began to have tarry stools. She was given 1,000 c.c. of whole blood intravenously and nasal oxygen. There were no localizing symptoms or severe pain. The abdomen was soft. She continued to vomit brownish-black material and to have tarry stools. She expired on June 6, approximately five days after delivery and nine days after admission to the hospital.

Postmortem Findings.—Pathologic examination of the gastrointestinal tract revealed no lesions grossly; however, microscopically, one site in the stomach showed necrosis with numerous bacteria in the mucosa. There were approximately 2,000 c.c. of bloody stool in the intestine. The kidneys were consistent with eclampsia. The spleen was acutely inflamed. Autopsy was not completed for the family withdrew their permission suddenly.

CASE 3.—M. D. was a white woman, aged 17 years, gravida i, para 0, serology negative. Her last menstrual period was April 15, 1944, and expected date of confinement was Jan. 26, 1945. Repeated urinalyses and blood pressure readings were normal during the prenatal course. The patient was apparently well until the morning of Dec. 4, 1944, at which time she complained of headaches and vomiting. At 7 P.M. on the same day the patient had sudden loss of vision.

On admission, the temperature was 99° F., pulse 70, respirations 22, blood pressure 190/150. The patient was in a semistuporous condition, and there was complete loss of

vision bilaterally. No hemorrhages, exudates, or vascular changes were noted in the fundi. The heart and lungs were negative. The abdomen was compatible with a thirty-six week's pregnancy. The patient was not in labor.

The patient was treated with hypertonic glucose solution, magnesium sulfate intravenously, Dilaudid and Luminal Sodium for sedation. Six hours after admission, she had a convulsion and the blood pressure was recorded as 260/140. Urine obtained by catheterization showed 4 plus albumin.

Twelve hours after admission, the patient was again catheterized and 100 c.c. of prune-juice-colored urine was obtained. This urine was examined spectroscopically and found to be methemoglobin. Blood smear at this time did not reveal any malarial parasites. Platelet count was 100,000. Red blood cell fragility test ranged from 0.48 per cent to 0.36 per cent. Spinal puncture was performed twelve hours after admission, and 100 c.c. of xanthochromic spinal fluid were removed under moderate pressure. Blood pressure following the puncture was 180/130. Hypertonic fluids and sedation were continued, and the blood pressure remained consistently elevated. Repeated urinalyses revealed 3 to 4 plus albumin, and the sediment was loaded with red blood cells.

Eighteen hours after admission, the patient's blood pressure was 140/120. At this time she had projectile vomiting of a coffee-ground material which was positive for occult blood. Blood pressure following this episode of vomiting was 140/120. She immediately started to have irregular uterine contractions, and the membranes were ruptured artificially at 2 P.M. on December 5. At 7 P.M. a stillborn fetus weighing 4 pounds 4 ounces was delivered by low forceps. Postpartum bleeding was minimal.

Despite hypertonic glucose solutions, magnesium sulfate, plasma, and whole blood the patient failed to show any satisfactory improvement. Blood pressure consistently remained elevated. Pulse was rapid and of poor quality. Urinary output continued to be minimal and consisted of dark-colored fluid. The patient's temperature gradually rose to 105° F. Vomiting of coffee-ground material continued. Blood nonprotein nitrogen showed a gradual rise, and, on December 5, the nonprotein nitrogen was 43. On December 7 and 9 the nonprotein nitrogen was 104 and 88 respectively. On December 11, the nonprotein nitrogen was 264. The patient expired on December 11, approximately eight days after admission and six days after delivery.

CASE 4.—I. L. S. was a 36-year-old Negro woman, gravida xiv, para xii, who entered the hospital on April 25, 1946, with a history of having had three convulsions. Her last menstrual period was Aug. 13, 1945, and her expected date of confinement was May 20, 1946.

The patient was an obese Negro woman in a semicomatose condition. Temperature 101° F., pulse 120, respirations 30, blood pressure 190/130. Ophthalmoscopic examination revealed marked arteriospasm with a small hemorrhage in the right retina at the upper margin of the macula. Uterus was compatible with the size of a thirty-six week's pregnancy. There was generalized edema of the lower extremities, of the hands, and of the face.

She was treated with sedation, Luminal Sodium, hypertonic glucose, magnesium sulfate, calcium chloride, and plasma transfusions. Urinalysis revealed 4 plus albumin with many fine and coarse granular casts. Nonprotein nitrogen on admission was 55 mg. The urine was bloody. On April 26, 1946, the patient had an episode of projectile vomiting of coffee-ground material which was positive for occult blood. At 10 P.M. the same day, the membranes were ruptured artificially in an effort to induce labor. She started to have uterine contractions and delivered a viable, premature male infant at 8 A.M. on April 27, 1946. Following delivery, the patient's blood pressure dropped to 150/100. She remained in a comatose condition. Temperature was 102° F., pulse 130, respirations 30. Penicillin therapy was instituted. Plasma and blood transfusions magnesium sulfate, hypertonic glucose, and nasal oxygen were continued. The edema gradually disappeared, and she began to respond. Her blood pressure appeared to be stabilized and remained at the level of 140/100. She was discharged on May 20, in good condition. Blood pressure at this time was 130/80, and the urine was negative for albumin and casts.

Comment

Three cases presented an eclamptic syndrome of hypertension, edema, convulsions, oliguria, and albuminuria. All four had severe projectile vomiting of blood, followed by marked decrease of blood pressure. In all, the onset of labor occurred 24 to 28 hours following the onset of projectile hematemesis. Three of the patients delivered stillborn infants, in which the fetal heart tones were not audible, following the onset of hematemesis. In one case, in which the patient survived, the infant was premature and viable.

Pathologic study of Case 1 revealed no specific source of hemorrhage in the esophagus or stomach in the form of varices. However, it was noted grossly that there were marked superficial destruction and ulceration of the mucosa of the stomach and esophagus. This may have been a source of bleeding, but it was not thought that it would have produced the amount of hematemesis noted clinically. The elevated temperature was probably due to the severe chronic endometritis in which there were necrosis and masses of bacteria in the endometrium. Together with this infection, she had acute pyelonephritis bilaterally and an acute splenic tumor. The liver showed none of the lesions considered pathognomonic of eclampsia.

This infection may have been the underlying cause of her massive hematemesis and the death of the fetus.

Case 2 was not completely autopsied, for the family withdrew their permission suddenly. The gastrointestinal tract, however, contained approximately 2,000 c.c. of bloody stool. No lesions were noted grossly, although microscopically one site in the stomach showed necrosis with numerous bacteria of the mucosa.

The kidneys demonstrated focal areas of inflammation and were consistent with eclampsia. The spleen was acutely inflamed.

Cases 3 and 4 did not come to autopsy. However, they were both eclamptic and ran a septic temperature.

The hemorrhagic tendency noted may be due to eclampsia or to infection. This hemorrhage may be similar to the intrauterine hemorrhage observed in premature separation of the placenta, and the association between the latter condition and toxemia of pregnancy has long been established. The death of the fetus may be attributed to the infection or to the severe gastrointestinal bleeding causing anemia and shock.

Summary

1. Four cases of severe gastric hemorrhage in pregnancy are presented.

2. There were three deaths and one survival.

3. Three cases presented an eclamptic syndrome of hypertension, edema, convulsions, oliguria, and albuminuria.

4. All four cases ran a septic temperature.

5. All four cases had severe projectile vomiting of blood followed by marked decrease of blood pressure.

6. In three of the four cases, the onset of labor occurred 24 to 28 hours following the onset of projectile hematemesis.

7. Three cases delivered stillborn infants, and, in one case, in which the patient survived, the infant was premature and viable.

References

1. Greely, A. V., and Stubenbord, W. D.: Am. J. Obst. & Gynec. 42: 154-156, 1941.
2. Preiss, E.: Gynaek. Rundschau, Berl. & Wien. 1: 725-727, 1907.
3. Sturrock, W. D.: Brit. M. J. 1: 218, 1913.
4. De Lee, J. B., and Greenhill, J. P.: The Principles and Practice of Obstetrics, ed. 8, Philadelphia, 1943, W. B. Saunders Company.

402 Farmington Avenue,
Hartford, Conn.

Department of Reviews and Abstracts

Selected Abstracts

Abortions

Licciardello, A. T., and Stanbury, J. B.: Acute Hemolytic Anemia From Quinine Used as an Abortifacient, New England J. Med. **238:** 120, 1948.

Acute hemolytic anemia following the administration of quinine has rarely been observed except in the presence of malaria. However, Terplan and Javert found eight cases in the literature. All these patients were women who had taken or been given quinine as an abortifacient. All died.

The authors report a patient who, two weeks after admission to the hospital, admitted having taken nine large capsules containing a white powder to interrupt a suspected pregnancy. The white powder proved to be quinine, as 1.3 mg. of quinine per liter were recovered from the urine on the day of her admission to the hospital.

Her hospital course was stormy, characterized by elevated temperature, jaundice, hemoglobinuria, albuminuria, nitrogen retention and a severe anemia, the result of hemolysis of her red blood cells. The patient recovered and was discharged on her 44th hospital day.

This report serves to call attention to the fact that quinine is an occasional cause of severe hemolytic anemia associated with jaundice and hemoglobinuria and to emphasize the danger of quinine as an abortifacient. JAMES P. MARR.

Fouracre-Barns, H. H.: Therapeutic Abortion by Means of Soft-Soap Pastes, Lancet, p. 825, Dec. 6, 1947.

The author slowly injects 15 to 20 c.c. of a warm soft-soap paste into the cervix, and, in 80 per cent of 71 pregnant women so treated, abortion occurred about 24 to 48 hours later. Four patients bled excessively and seven were morbid. There were no deaths.

The article recommends this method for interrupting pregnancy in cardiac and pulmonary diseases, wherein general anesthesia is hazardous. IRVING L. FRANK.

Corston, J. McD., and Stallworthy, John: The Treatment of Inevitable, Incomplete, and Septic Abortion, Brit. M. J., p. 89, July 19, 1947.

Management of incomplete abortion by conservative measures versus prompt surgical evacuation of the uterus is discussed. The authors favor the latter method, and describe the details as applied to 600 patients admitted to the Radcliffe Infirmary with a diagnosis of incomplete or inevitable abortion. The procedure followed is to take the patient to the operating room where she is anesthetized with thiopentone and the vulva and vagina swabbed with 1:1000 flavine solution. The patient is then examined and 0.5 mg. of ergometrine is injected into the cleaned cervix. If necessary, the cervix is dilated. Retained products are removed by sponge forceps and a blunt flushing curette. The uterus is then packed with a 2 inch gauze pack which is removed six hours later. Forty-two of the total cases were infected on admission. In these cases, sulfonamide therapy was started prior to the operative procedure and the pack was impregnated with sulfathiazole powder. Seventy-one blood transfusions were

employed. Patients were frequently discharged on the third or fourth day, but the average hospital stay was seven and one-half days. There was one death, a patient moribund on admission, who had been ill a month. Necropsy revealed a generalized *Cl. welchii* septicemia. The authors believe the results superior to the conservative method of treatment.

R. G. DOUGLAS.

Cesarean Section

Smith, William P.: Cesarean Section Seven Years After Hemi-Hysterectomy in a Bicornuate Uterus, Am. J. Surg. **74:** 856, 1947.

The author briefly reviews congenital uterine malformations and then reports an interesting case of pregnancy following an operation for a bicornuate uterus. This patient was first seen at the age of 13 years after a diagnosis of rectal abscess had been made and a rectal incision made for its drainage. The abnormality proved to be that of a bicornuate uterus with one cervix connected with the right uterine cavity, the left cavity having no cervical canal; this left cavity had developed a hematometra with the child's menarche, and this was infected with the attempt at drainage through the rectum. A laparotomy was finally performed and the left half of the uterus removed.

The patient menstruated normally thereafter, and eventually married and became pregnant at the age of 20 years. Pregnancy proceeded uneventfully and the patient was delivered by cesarean section in her eighth month. The operator noted the left uterine wall to be thinned; the threat of possible rupture in labor is emphasized.

S. B. GUSBERG.

Heffernan, Roy J., and Sullivan, Charles Leavitt: Which Type Cesarean Section? New England J. Med. **238:** 241, 1948.

This concise informative article on the value of the different types of cesarean section is based on the long experience of the authors and their extensive collection of sound statistical information.

Beginning with the classical cesarean section, since it is the oldest type, they found 15,030 patients who had been subjected to the classical operation. The mortality was 3.87 per cent, a most significant finding.

Notwithstanding better obstetric management, improved operative technique, replacement of blood, and chemotherapy and the antibiotics, peritonitis still occurs. The authors agree that this type of abdominal delivery has so many disadvantages that it should be used only when better methods are not applicable or when the uterus is to be removed.

In a series of 14,776 low flap or low-cervical cesarean sections, the mortality was 1.52 per cent. It is, therefore, apparent that the lower segment operation is over twice as safe as the classic operation.

The authors find the lower-segment operation a very satisfactory type of abdominal delivery in uncomplicated, clean cases, but not without danger in the potentially infected case, since it does not ensure protection against peritonitis from the spill or seepage of infected uterine contents.

They point out that the lower-segment cesarean is usually a safe and satisfactory procedure when done electively, when the patients have been in labor ten hours or less, with intact membranes, or where there has been no vaginal examination, or membranes ruptured longer than six hours.

For the potentially infected parturient, Heffernan and Leavitt perform the extraperitoneal cesarean section. Their indications for this procedure are: 1. the slightest suspicion of infection, 2. ruptured membranes for a period of eight hours, 3. labor of more than six hours' duration, and 4. cases where repeated rectal or vaginal examinations have been made.

In a series of 1089 modern extraperitoneal cesarean sections the mortality was 0.82 per cent. Four patients succumbed to sepsis and two to postoperative hemorrhage.

The authors report 72 extraperitoneal cesareans from their own experience. There was no fetal or maternal mortality. With excellent illustrations, they describe in detail their technique in performing this lifesaving operation.

Both authors reject cesarean hysterectomy for infection, revealing a maternal mortality of 14.2 per cent in 119 such operations. Their rejection is due also to the loss of the reproductive organ, which the operation entails, besides the shock and additional blood loss at the time of the operation. They reserve a place for cesarean hysterectomy, however, for those patients with multiple fibroids, atonic uterus, or other pathologic conditions of the uterus.

They report the experience of Baird, a maternal mortality of 7 per cent in 147 cases necessitating craniotomy, only to condemn craniotomy on the living child.

They conclude that the modern extraperitoneal cesarean section is not only the safest method for the infected or potentially infected parturient patient but also may be used to advantage for less imperative indications. JAMES P. MARR.

Gray, T. Cecil: d-Tubocurarine in Cesarean Section, Brit. M. J. 1: 444, April 5, 1947.

The technique employed in anesthetization of 30 patients for cesarean section is described. 0.65 mg. of atropine is given one hour before operation. d-Tubocurarine (Tubarine, Burroughs Wellcome & Co.), 15 mg. is injected, with the patient on the table, followed by 0.3 Gm. Kemithal (cyclohexenyl-allyl-thiobarbiturate) in 5 per cent solution. (Technique not stated.) "Closed circuit" cyclopropane anesthesia is then commenced at once. The operation may be started as soon as the patient fails to respond to painful stimuli. An airway is not employed because of the light anesthesia. Vomiting is avoided by this means. No evidence of curarization was evident in the babies. The uterus contracted so firmly that the use of Pituitrin was abandoned. Because of the light anesthesia the patient usually "awakens" as the dressings are applied. Postoperative complications were minimal.

The author believes the results warrant the exploration of the possibilities of this form of anesthesia by others. R. G. DOUGLAS.

Newborn

Wiener, A. S., Wexler, I. B., and Grundfast, T. H.: Therapy of Erythroblastosis Fetalis With Exchange Transfusion, Bull. New York Acad. Med. 23: 207, 1947.

In 1925 Hart successfully treated a case of icterus gravis by exchange transfusion. These authors first employed exchange transfusions in 1944 on an infant with mongolian idiocy. In this, and in a subsequently treated case of icterus gravis, coagulation interfered seriously with withdrawal of blood. In 1946, following Wallerstein's encouraging results in erythroblastosis, the authors again used exchange transfusions, after heparinization of the infant's blood. Three 200 unit doses of heparin are used during the exchange. In seventeen cases known to the authors, heparin has proved innocuous, and does not magnify possible silent intracranial hemorrhages (which Wallerstein considered a dangerous possibility).

The infusion enters the saphenous vein, while blood is draining from the radial artery. The total exchange is twice the total blood volume (or, about 500 c.c.), which results in 90 per cent substitution. Success depends on the fate of the remaining Rh-positive cells. If lysis occurs, no harm results. If clumping occurs, the circulation is obstructed, and the procedure has been a failure. To avoid clumping (intravascular conglutination), the authors suggest that the conglutinin content of the donor blood be reduced by replacing one-half the plasma by saline. Polycythemia from overtransfusion should be avoided. IRVING L. FRANK.

Exsanguination-Transfusion in Erythroblastosis Fetalis, Internat. Med. Digest 50: 246, 1947.

Exsanguination-transfusion, or the exchange of good blood for bad, was first proposed in 1921. At that time Robertson reported its use in the treatment of severe burns in infants and children, and later in treatment of erysipelas, septic scarlatina and acute intestinal intoxication. Subsequently others used it in the treatment of poisoning by resorcin, mercuric chloride and phenol, and in treatment of typhoid fever.

The collected results of Rh-negative transfusion in the treatment of erythroblastosis have not sustained early enthusiasm. The procedure of exsanguino-transfusion, which had been suggested in 1932 for this condition by Diamond, Blackfan and Baty, has therefore been called into use. Wallerstein, in a pioneer report on 9 cases thus treated, has given evidence adequate to show that the procedure is superior to the simple transfusion of Rh negative blood. It is emphasized that substitution transfusion should be used in the preicteric period soon after birth, before damage to the brain and liver has advanced too far. IRVING L. FRANK.

Wallerstein, H.: Substitution Transfusion: A New Treatment for Severe Erythroblastosis Fetalis, Am. J. Dis. Child. **19:** 73, 1947. (From a long abstract in *International Medical Digest* **50:** 235 1947.)

The outlook in erythroblastosis fetalis has been somewhat improved by premature induction of labor, and by repeated transfusions of Rh-negative blood. Some babies, however, have succumbed with deepening jaundice, despite these transfusions. Further treatment should be designed to remove the products of hemolysis, and to prevent their formation by the removal of the Rh-positive erythrocytes before they can be destroyed in large numbers by the maternal antibody.

Subtotal replacement of the infant's circulating blood may be carried out by removing 50 c.c. portions of blood (by syringe from the superior longitudinal sinus), in alternation with 50 c.c. blood infusions (which are added to a continuous saline or plasma infusion in an arm vein). Through five such exchanges only 80 c.c. remains of the original 250 c.c. blood volume. A supplemental 100 c.c. of Rh-negative blood is given, which further reduces the original Rh-positive blood to 25 per cent of the starting volume. Continuous simultaneous exsanguination-transfusion may be carried out by permitting the cannulized radial artery to bleed, and regulating the blood infusion to match the bleeding rate. After a 250 c.c. replacement, only 36.7 per cent of the original blood remains.

When used after toxic manifestations have become pronounced the benefits of this procedure are minimized. Substitution transfusion is recommended chiefly as a prophylactic measure, and if used in the subicteric period immediately after birth, it prevents damage to the liver and brain. The history of erythroblastosis in a previous infant is emphasized as the important indication for prophylactic treatment. At the time of delivery, icteric amniotic fluid, large pale placenta, or erythroblastosis of the cord blood may suggest the preicteric phase and indicate early treatment. If, on the basis of these criteria, one anticipates that severe erythroblastosis may develop, it is best that substitution transfusion be given as soon as possible after birth. IRVING L. FRANK.

Wallerstein, Harry: Substitution Transfusion: A New Treatment for Severe Erythroblastosis Fetalis, Am. J. Dis. Child. **73:** 19, 1947.

Erythroblastosis fetalis has long been recognized as a hemolytic disease of unknown origin with varying degrees of anemia and hepatic damage.

Therapy, even before the recent elucidation of the pathogenesis, was directed at correction of the anemia by repeated transfusions.

Since 1941 refinement in the treatment of erythroblastosis, based on the role of the Rh factor, have resulted in a decidedly improved prognosis.

The significance of hepatic damage induced by excessive red blood cell hemolysis and the accompanying reactive liver erythropoiesis made it evident that a new and radically different approach to the therapy of erythroblastosis was required.

The procedure consists of the actual withdrawal of the infant's Rh-positive cells and their replacement with innocuous Rh-negative erythrocytes. In order to avoid subjecting the child to the dangers of shock from exsanguination, the withdrawal and replacement are carried out simultaneously. The differential typing of cells removed at the beginning and at the end of the exchange confirms the fact that only 20 to 25 per cent of the original Rh-positive erythrocytes remained.

A technique is given and seven cases are reported. JAMES P. MARR.

Puerperium

Coryell, M. N., Harris, M. E., Miller, S., Williams, H. H., and Macy, I. G.: Metabolism of Women During the Reproductive Cycle XIV. The Utilization of Pantothenic Acid During Lactation, J. Lab. & Clin. Med. 32: 1454, Dec., 1947.

Metabolic studies of pantothenic acid intake and output were carefully performed in lactating women. The output in milk and urine was measured during the immediate puerperium and also at a later period, when lactation was well established. During the first ten postpartum days, pantothenic acid secretion in the milk was constant, its steady total increase being related to increasing milk volume produced. During the first five-day period, most subjects excreted less pantothenic acid in the urine than they took in their diet, while the reverse was true in the second five-day period. The authors conclude that pantothenic acid may be stored in the body or that it may be retained for more than twenty-four hours during its metabolism. They also state that physiologic levels are maintained in the milk and urine of such women, without respect to their current intake, if their nutritional status in respect to vitamins is good. S. B. GUSBERG.

Coryell, M. N., Harris, M. E., Miller, S., Rutledge, M. M., Williams, H. H., and Macy, I. G.: Metabolism of Women During the Reproductive Cycle. XV. The Utilization of Biotin During Lactation, J. Lab. & Clin. Med. 32: 1462, 1947.

Careful metabolic studies of biotin intake and output in urine and milk were made in lactating women. The values for biotin in breast milk during the first four postpartum days were too low to be reliable. During the second five-day period, the total secretion and relative concentration in the milk varied widely. Studies of milk obtained at later periods, when lactation was well established revealed it to contain 2 to 14 per cent of the total intake. The urinary biotin excretion averaged 47 per cent of the intake during this period. The authors cite the work of other investigators, who have demonstrated a fecal biotin factor in biotin metabolism; they suggest that variation in fecal synthesis may explain the variability of individual response. S. B. GUSBERG.

Correspondence

Death From Placenta Previa

To the Editor:

I have read with interest the case reported by Dr. Brody under Correspondence in the February, 1948, issue of the JOURNAL, purporting to be a death due to placenta previa in which there was neither intrauterine nor intracervical manipulation.

A copy of Dorland's Medical Dictionary has been sent to Dr. Brody for his effort and thoughtfulness in trying to find a case of placenta previa, uncomplicated by accreta, as mentioned in my paper, in which there had been neither intracervical nor intrauterine manipulation, but which, nevertheless, terminated in death. Obviously, sudden or immediate exitus in placenta previa has only one cause—such loss of blood as is incompatible with life. In many cases of sudden death in obstetrics, autopsy findings are necessary to determine whether the death was due to hemorrhage, or partially to hemorrhage, with shock being the major element.

Unfortunately, for two reasons, I cannot use this case to start my series: (1) There is no definite proof that the case was one of placenta previa, and (2) there is no proof that the patient died from hemorrhage. These points will be discussed.

Dr. Brody states: "At midnight she began to feel abdominal pains and discomfort, which became rapidly worse. She was rushed to the hospital." On admission to the hospital she was "cyanotic with labored breathing." Examination "revealed a full-term uterus which was hard and tender. Fifteen minutes later, while the patient was being shaved, she had a profuse hemorrhage from the vagina; . . . one-half hour after . . . she was in complete shock, restless, tossing in bed, and gasping for breath. Plasma was administered . . . the patient expired twenty minutes later." It would be most unfair to assume that the plasma had anything to do with the exitus of this shocked but restless and tossing patient who expired twenty minutes after the intravenous therapy.

The autopsy findings showed "congestion and edema of the lungs," which are common in shock, "a full-term fetus in utero, and a placenta lying in the lower pole[?] of the uterine cavity." There was no reported careful examination, such as microscopic sections to show the real attachment site of the placenta; nor whether the abdominal viscera were pale or edematous with subcapsular petechial hemorrhages.

In contradistinction to the foregoing facts reported for Dr. Brody's case, and leaving your readers to draw their own conclusions, it might be in order to state that the amount of bleeding at any given period in labor, or before labor in a case of placenta previa, depends entirely on the cervical effacement and dilatation with its consequent placental separation; placenta previa is unaccompanied by pain, uterine tenderness, or hardness; and, if the loss of blood were to become lethal, autopsy findings would be that of what is commonly designated "bled white," i.e., none of the viscera, including the lungs, would show any evidence of edema, but would be pale in color. The labored breathing indicated that pulmonary edema was present prior to death. No attempt was made to explain the hyperpyrexia.

It seems to me that Dr. Brody was unfortunate in encountering a fatal case of premature separation of the placenta regardless of the latter's site of attachment. The separation was sudden and massive and gave rise to the clinical symptoms as described by him and followed rapidly by death. The autopsy finding of edema of the lungs tends to confirm the opinion that death was due to shock and not to loss of blood. And it should be mentioned that in massive ablation of the placenta such as occurred in this case, shock is a much more common cause of death than hemorrhage. For confirmation of these opinions, I would suggest that Dr. Brody consult Sheehan[1] or Moon.[2] Both are eminent authorities on deaths due to shock.

Since the publication of my paper, "The Conservative Management of Some Varieties of Placenta Previa," three years ago, approximately 7,500,000 babies have been born in continental United States. Assuming that the incidence of placenta previa is 1 in 180 term or near-term deliveries, there should have been 41,666 cases of all varieties of previa during this time. I am still sure that some of these cases, apart from those of placenta previa accreta, have, without manipulation, "bled to death," and I am still going to endeavor to find some of these cases in order to determine its incidence. With our better medical recording and with proper assistance from the numerous Maternal Mortality Committees, and, may it be added, with the same interest as shown by Dr. Brody, some cases should be uncovered. I am still of the opinion that the textbook picture of placenta previa is too frightening, and that the doctor who quickly says, "Oh, I know of a case, etc.," is probably dealing more in folklore than in facts.

I hope the publication of this correspondence will stimulate further interest.

HERMAN W. JOHNSON, M.D.

DEPT. OF OBSTETRICS,
BAYLOR UNIVERSITY
COLLEGE OF MEDICINE,
HOUSTON, TEXAS,
March 8, 1948.

References

1. Sheehan, H. L.: J. Obst. & Gynaec. Brit. Emp. **16:** 218-231, 1939.
2. Moon, V. H.: Shock, Its Dynamics, Occurrence and Management, Philadelphia, 1942, Lea and Febiger.

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

American Gynecological Society. (1876) *President,* Ludwig Emge. *Secretary,* Norman Miller, Ann Arbor, Mich. Next meeting, May, 1949, Hot Springs, Va.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons. (1888) *President,* A. D. Campbell, Montreal, Quebec. *Secreatry,* James R. Bloss, 418 11th Street, Huntington, W. Va. Annual meeting Hot Springs, Va., Sept. 4-6, 1947.

Central Association of Obstetricians and Gynecologists. (1929) *President,* Earl C. Sage, Omaha, Neb. *Secretary-Treasurer,* John I. Brewer, 104 South Michigan Ave., Chicago, Ill. Annual meeting Louisville, Ky., Oct. 23, 24, and 25, 1947.

South Atlantic Association of Obstetricians and Gynecologists. (1938) *President,* S. R. Norris, Jacksonville, Fla. *Secretary,* E. D. Colvin, 1259 Clifton Road, N.E., Atlanta, Ga. Annual meeting at Williamsburg, Va., February 10 to 12, 1949.

A. M. A. Section on Obstetrics and Gynecology. *Chairman,* William F. Mengert, Dallas, Texas. *Secretary,* A. B. Hunt, Mayo Clinic, Rochester, Minn. Annual meeting June, 1947.

New York Obstetrical Society. (1863) *President,* Albert H. Aldridge. *Secretary,* Claude E. Heaton, 205 East 69th St., New York 21, N. Y. Second Tuesday, from October to May, Yale Club.

Obstetrical Society of Philadelphia. (1868) *President,* John B. Montgomery. *Secretary,* James P. Lewis, 1930 Chestnut St., Philadelphia, Pa. First Thursday, from October to May.

Chicago Gynecological Society. (1878) *President,* Aaron E. Kanter. *Secretary,* Edward M. Dorr, 30 N. Michigan Ave., Chicago 2, Ill. Third Friday, from October to June, Hotel Knickerbocker.

Brooklyn Gynecological Society. (1890) *President,* Alexander E. Dunbar. *Secretary,* William T. Daily, 142 Joralemon St., Brooklyn, N. Y. First Friday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn, N. Y.

Baltimore Obstetrical and Gynecological Society. (1929) *President,* Lawrence Wharton. *Secretary-Treasurer,* John W. Haws, 9 E. Chase St., Baltimore, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.

Cincinnati Obstetrical Society. (1876) *President,* Stanley T. Garber. *Secretary,* Joseph G. Crotty, 146 West McMillan St., Cincinnati, Ohio. Third Thursday of each month.

Louisville Obstetrical and Gynecological Society. *President,* W. O. Johnson. *Secretary,* W. E. Oldham, 842 Barrett Avenue, Louisville, Ky. Meetings fourth Monday of each month from September to May, Brown Hotel.

Portland Society of Obstetrics and Gynecology. *President,* Ronald Frazier. *Secretary-Treasurer,* Gifford D. Seitz, 919 Taylor St. Bldg., Portland 5, Ore. Meetings last Wednesday of each month.

Pittsburgh Obstetrical and Gynecological Society. (1934) *President,* James Hodgkiss. *Secretary,* Clarence H. Ingram, Jr., 902 Peoples East End Building, Pittsburgh 6, Pa. First Monday of October, November, December, January, February, March, April, and May.

Obstetrical Society of Boston. (1861) *President,* Paul Gustafson. *Secretary,* H. Bristol Nelson, 1180 Beacon Street, Brookline, Mass. Third Tuesday, October to April, Harvard Club.

New England Obstetrical and Gynecological Society. (1929) *President,* Arthur E. G. Edgelow, Springfield, Mass. *Recorder,* Carmi R. Alden, 270 Commonwealth Ave., Boston 16, Mass. Meetings held in May and December.

Pacific Coast Obstetrical and Gynecological Society. (1931) *President,* Henry N. Shaw. *Secretary-Treasurer,* William Benbow Thompson, 6253 Hollywood Blvd., Los Angeles, Calif. Next meeting in Seattle, Wash., Oct. 1 to 4, 1947.

Washington Gynecological Society. (1933) *President,* William J. Cusack. *Secretary,* John Parks, 901 23 St., N.W., Washington, D. C. Fourth Saturday, October, November, January, March, May.

New Orleans Obstetrical and Gynecological Society. (1924) *President,* Woodward D. Beacham. *Secretary,* Harry Meyer, Audubon Bldg., New Orleans 16, La. Meetings held October, November, January, March, and May.

St. Louis Gynecological Society. (1924) *President,* Joseph A. Hardy, Jr. *Secretary,* Paul F. Fletcher, 634 North Grand Ave., St. Louis 3, Mo. Meetings second Thursday, October, December, February, and April.

---

*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the Society's name is the year of founding.

San Francisco Gynecological Society. (1929) *President,* Albert M. Vollmer. *Secretary,* Daniel G. Morton, University of California Hospital, San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.

Texas Association of Obstetricians and Gynecologists. (1930) *President,* Warren E. Massey. *Secretary,* George F. Adam, 4115 Fannin St., Houston 4, Tex.

Michigan Society of Obstetricians and Gynecologists. (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President,* Harold C. Mack. *Secretary,* John P. Ottaway, 1551 Woodward Ave., Detroit, Mich. Meetings first Tuesday of each month from October to May (inclusive).

Central New York Association of Obstetricians and Gynecologists. (1938) *President,* Raymond J. Pieri. *Secretary,* Nathan N. Cohen, 713 E. Genesse St., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May.

Alabama Association of Obstetricians and Gynecologists. *President,* Gilbert F. Douglas. *Secretary,* Hunter Brown, 1922 South Tenth Ave., Birmingham, Ala.

San Antonio Obstetric Society. *President,* I. T. Cutter. *Secretary,* S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.

Seattle Gynecological Society. (1941) *President,* Roger E. Stewart. *Secretary,* Albert F. Lee, 1115 Boylston, Seattle 1, Wash. Meetings held on third Wednesday of each month.

Denver Obstetrical and Gynecological Society. (1942) *Secretary,* Emmett A. Mechler, 1612 Tremont St., Denver, Colo.

Wisconsin Society of Obstetrics and Gynecology. (1940) *President,* J. M. Freeman. *Secretary-Treasurer,* Lionel T. Servis, 425 East Wisconsin Ave., Milwaukee. Meetings held in May and October.

San Diego Gynecological Society. (1937) *President,* R. C. Hall. *Secretary,* D. Dalton Deeds, 2001 Fourth Ave., San Diego, Calif. Meetings held on the last Wednesday of each month.

North Dakota Society of Obstetrics and Gynecology. (1938) *President,* Ralph E. Leigh, Grand Forks. *Secretary,* G. Wilson Hunter, 807 Broadway, Fargo, N. D.

Virginia Obstetrical and Gynecological Society. (1936) *President,* John Boyd. *Secretary-Treasurer,* William Durwood Suggs, Monument Ave. and Lombardy St., Richmond, Va. Next meeting not announced.

Columbus Obstetric and Gynecologic Society. (1944) *President,* Dana Cox. *Secretary,* Zeph J. R. Hollenbeck, 9 Buttles Ave., Columbus, Ohio. Meetings held fourth Wednesday of each month.

Naussau Obstetrical Society. (1944) *President,* Austin B. Johnson. *Secretary,* Robert S. Millen, Westbury, N. Y. Meetings, bimonthly from October to May.

Bronx Gynecological and Obstetrical Society. (1924) *President,* H. J. Lesnick. *Secretary,* Mark Daniel, 2344 Davidson Ave., Bronx 53, N. Y. Meetings, fourth Monday monthly from October to May.

Washington State Obstetrical Society. (1936) *President,* John H. Fiorino, Everett. *Secretary,* H. H. Skinner, Yakima, Meetings, first Saturday of April and October.

Kansas City Obstetrical and Gynecological Society. (1922) *President,* Thomas J. Sims. *Secretary,* LeRoy Goodman, 702 Bryant Bldg., Kansas City, Mo. Meetings, last Thursday, September, November, January, and March; first Thursday, May, University Club.

Los Angeles Obstetrical and Gynecological Society. (1914) *President,* Carl E. Krugmeier. *Secretary-Treasurer,* A. M. McCausland, 3780 Wilshire Blvd., Los Angeles, Calif.

North Carolina Obstetrical and Gynecological Society. (1932) *President,* Wallace B. Bradford. *Secretary,* Richard B. Dunn. Meetings semiannually.

The Society of Obstetricians and Gynecologists of Canada. (1944) *President,* William A. Scott. *Secretary,* James Goodwin, 516 Medical Arts Bldg., Toronto, 5. Meetings held annually, date of next meeting to be announced later.

Akron Obstetrical and Gynecological Society. (1946) *President,* S. B. Conger. *Secretary-Treasurer,* Alven M. Weil, 1030 First National Tower, Akron 8, Ohio. Meetings held third Friday of January, April, July, and October, City Club of Akron, Ohio, Bldg.

Minnesota Society of Obstetrics and Gynecology. *President,* Everett C. Hartley. *Secretary,* John Haugen, 100 E. Franklin Ave., Minneapolis, Minn. Meetings held spring and fall.

Miami Obstetrical and Gynecological Society. (1946) *President,* M. C. Wilson. *Secretary,* George A. Mitchell, Huntington Bldg. Meetings, second Thursday in January, March, May, and November.

Omaha Obstetrical and Gynecological Society. (1947) *President,* Charles F. Moon. *Secretary,* Donald C. Vroman, 813 Medical Arts Bldg., Omaha 2, Neb. Meetings held third Wednesday in January, March, May, September, November.

Oklahoma City Obstetrical and Gynecological Society. (1940) *President,* Le Roy H. Sadler. *Secretary-Treasurer,* John W. Records, 301 Northwest 12 Street, Oklahoma City.

Cleveland Obstetrical and Gynecological Society. (1947) *President,* Robert E. Faulkner. *Secretary,* G. Keith Folger, 10515 Carnegie Ave. Meetings on fourth Tuesday of September, November, January, March, and May at University Club, 3813 Euclid Ave., Cleveland 15, Ohio.